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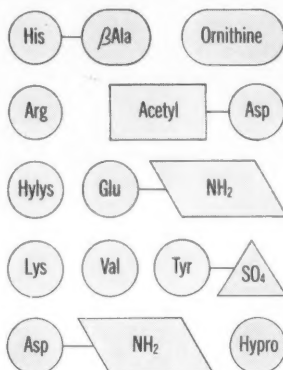
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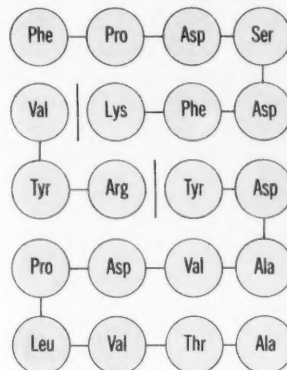
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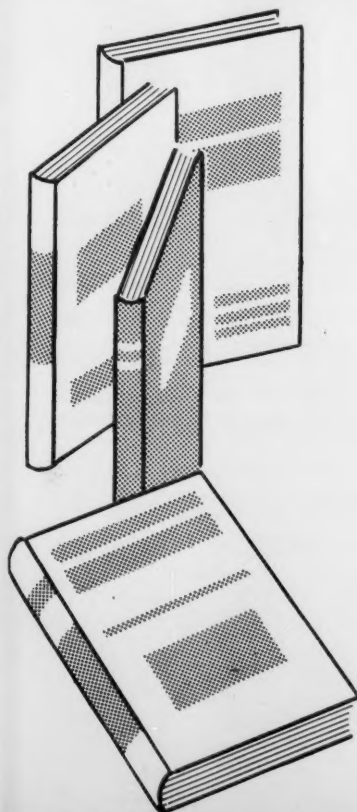
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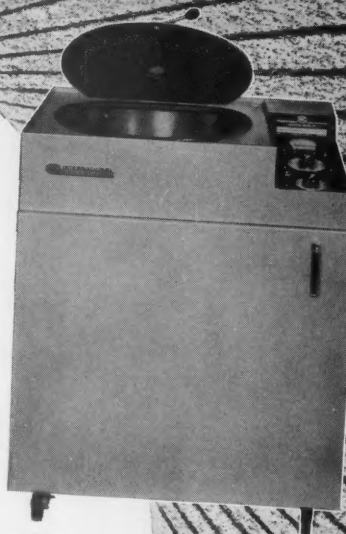
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## The Jinni in the Bottle

J. R. Wiggins, editor of the *Washington Post and Times Herald*, has been asking some of his scientist friends: If you could put the jinni back into the bottle, would you do it? Would you, if you had the choice, undo the work that led to the release of atomic energy? The question is not historical, for obviously the past cannot be undone. Neither is it a strictly scientific question, for if Otto Hahn, Lise Meitner, Enrico Fermi, and their collaborators had not released the atomic jinni, others would have. The point of the question is its social significance, not only for atomic energy itself, but also as a forewarning of problems that may lie ahead. Consider the moral, social, and political dilemmas that would follow upon ability to control the weather on a world-wide scale, to control genetic material, or to control human behavior.

Warren Weaver posed essentially the same question, in a somewhat more manageable form, in asking C. P. Snow, after his address at the 1960 AAAS annual meeting: If a scientist can see with reasonable clarity that continuing a particular line of research is likely to produce information that might be turned to evil ends, should he continue, or should he stop? When phrased in this way, the question poses a personal choice, but only a personal one. A particular scientist can avoid personal responsibility for findings that may be used for evil purposes. But he cannot prevent those findings from being made. If he stops, someone else will continue.

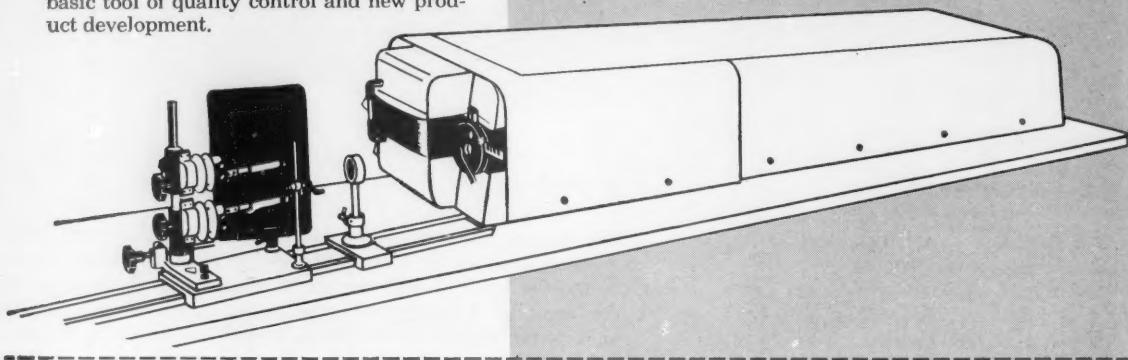
Among the several answers made to these questions is the statement that the scientist plays two roles, one as scientist and the other as citizen, and that he can and should keep the two roles separate. The distinction goes beyond saying that scientists should be concerned with the social implications of their work to say that the scientist, acting as a scientist, can press on wherever and as far as his curiosity and ability lead and permit, and that the same person, now acting as a citizen, can forget his scientific interests in helping to make decisions concerning science and its applications and its control. This is a comforting doctrine, but is it any more realistic than to expect the scientist to open all the bottles to see what they contain while the same person, as citizen, leaves firmly stoppered any that contains an ugly jinni?

Quite aside from the impossibility of undoing the past, and quite aside from the impossibility of preventing others from doing what a particular person refrains from doing, can we expect the scientist—not an idealized abstraction but the human being in the next office—to differentiate his role as a scientist from his role as a citizen? We do not expect the clergyman to forget his cloth when he goes to vote. Nor do we ask the member of another profession to stop and ask himself: Am I acting as a member of my profession or as a citizen of my country? What can we fairly ask of a scientist?

Would you put the jinni back into the bottle if you could? The question can start a lively discussion. It can also lead to a perplexing consideration of whether or not the scientist can separate his roles. —D.W.

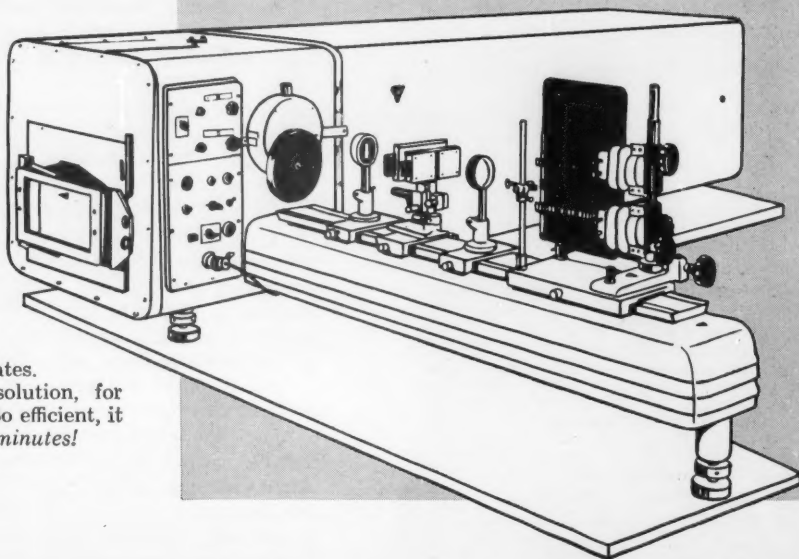
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## CURRENT PROBLEMS IN RESEARCH

Freezing Nuclei, Meteors,  
and RainfallDo tiny particles from meteor streams influence  
rainfall over the earth's continents?

N. H. Fletcher

New theories concerning mechanisms that exert a controlling influence upon the earth's weather are bound to be regarded with skepticism, particularly by meteorologists used to watching the orderly, though regrettably rather unpredictable, progression of cyclones and anticyclones, cold and warm fronts, over the earth's surface. Such indeed was the reception accorded the suggestion by E. G. Bowen, chief of the Radiophysics Division of the Australian Commonwealth Scientific and Industrial Research Organization, that there was a close connection between the earth's passage through meteor swarms and the whole terrestrial rainfall pattern some 30 days later.

In the eight years which have elapsed since the meteor hypothesis was first propounded it has excited sufficient interest and controversy that a great deal of experimental and statistical work has been undertaken in various parts of the world, designed to test the predictions of the theory and to extend our knowledge of the various links in the chain by which the mechanism is supposed to operate. Some of this work has already yielded interesting and important new information, while some experiments are still in the planning stages, and still others have revealed further puzzles for later investigation.

## Condensation Nuclei and Clouds

To view the meteor hypothesis in proper perspective we need first to see what is at present known about the way in which clouds form and the way in which rain develops within them.

When warm moist air rises it expands and cools, and its relative humidity increases toward 100 percent; at this stage the air is said to be saturated with respect to water vapor. Any further cooling of the air would cause a further increase in humidity above 100 percent, and the air would become supersaturated if it were perfectly clean, but in the atmosphere this does not happen. Instead, water begins to condense on some of the numerous tiny particles of soluble material which are normally suspended in the atmosphere, and a cloud of tiny water droplets begins to form at a relative humidity just greater than 100 percent. In fact, even in very fast growing clouds, the supersaturation rarely exceeds 1 percent.

These soluble particles on which the water droplets form are called condensation nuclei and are produced by evaporation of tiny droplets of sea water, or, even more importantly, by the actions of dew and sunshine on soluble salts in the soil. The concentration of condensation nuclei in the

atmosphere is normally quite large, and since their most important source is the soil, they are more numerous in air masses which have spent many days over a large continental land mass than in maritime air masses. Figure 1 shows the concentrations of condensation nuclei which become active at various supersaturations, as measured by Twomey in southeastern Australia.

When the condensation process is studied for different sets of possible conditions it is found that the maximum supersaturation reached is a few tenths of 1 percent, and from Fig. 1 this would lead us to expect that maritime clouds would have about 50 droplets per cubic centimeter, whereas continental clouds would typically have about 300 droplets per cubic centimeter. These values agree very closely with the results of droplet counts in clouds of maritime and continental origin reported by Squires.

Another thing which has been established is that in almost all reasonably large clouds, irrespective of size or origin, the liquid-water content averages about 0.5 gram per cubic meter. There appears to be some sort of mixing-in of dry air from outside the cloud which maintains this value. Taken with the droplet counts given above, this means that maritime clouds contain small numbers of rather large droplets, whereas continental clouds consist of large numbers of very small droplets.

Now, careful theoretical work by Hocking in England has shown that because of the complicated flow of air around small cloud droplets, only droplets with radii greater than about 18 microns are able to collide with each other; smaller drops deflect each other and can suffer only "near misses." Because of this effect, though the droplets of maritime clouds are big enough to form raindrops by repeated collisions and coalescences, most continental clouds are quite stable, in this respect,

The author is a senior lecturer in physics at the University of New England, Armidale, New South Wales, Australia.

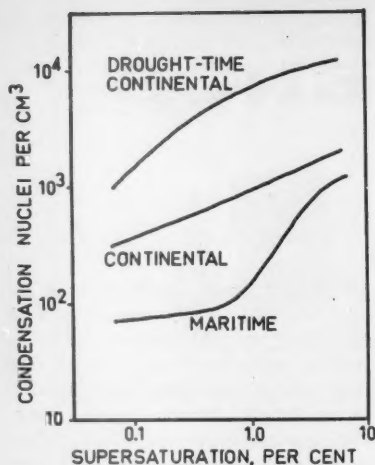


Fig. 1. Activity distributions of condensation nuclei in air masses of continental and maritime origin. [After Twomey]

have few such collisions, and can never yield rain by this mechanism. Since most important continental rainfall, with the exception of that falling on coastal regions, tends to originate in continental air masses, I shall now concentrate on the properties of these apparently stable clouds.

### Freezing Nuclei and Ice Crystals

As a cloud rises above the condensation level its top continues to cool, and eventually its temperature falls below the freezing point. It might be expected that the cloud droplets would then freeze to form tiny ice crystals, but this is not the case, and in fact tiny droplets of pure water can be supercooled to temperatures near  $-40^{\circ}\text{C}$  before they will freeze spontaneously. The presence of small particles, usually called freezing nuclei (*1*), is required to initiate ice formation in clouds at temperatures higher than this.

These freezing nuclei also occur naturally in the atmosphere, but whereas condensation nuclei are present in hundreds per cubic centimeter, the concentration of natural freezing nuclei active above  $-20^{\circ}\text{C}$  is only a few per liter of air. The general form of the activity spectrum of these natural freezing nuclei is shown in Fig. 2.

We may expect, then, that under average conditions, when cloud-summit temperature falls to  $-20^{\circ}\text{C}$ , the cloud top itself will contain about one ice crystal per liter. Though the con-

centration of these ice crystals is negligible as compared with that of water droplets, their physical importance is very great. At temperatures below  $0^{\circ}\text{C}$  the water-vapor pressure over ice is less than that over water, and at temperatures in the range  $-10^{\circ}$  to  $-20^{\circ}\text{C}$  this effect is so great that water droplets near one of these ice crystals evaporate quite quickly and the vapor is deposited upon the growing ice crystal. This process is illustrated in Fig. 3.

Here, then, is the process which leads to instability and precipitation in continental clouds. The ice crystals grow at the expense of neighboring water droplets until they are large enough to fall through the cloud, collecting further water droplets by collision as they do so. Whether the precipitation falls as rain, hail, or snow depends largely upon the total depth of the cloud and upon the temperature at its base. The concentration of ice crystals required to cause substantial precipitation from an average cloud is estimated to be between 1 and 10 per liter at the cloud top.

I might digress a moment to point out that this is the origin of our present rain-making techniques. Silver iodide smoke is a very efficient ice-nucleating agent at temperatures below about  $-10^{\circ}\text{C}$ ; hence, if this smoke is injected into a cloud it starts the precipitation mechanism operating much earlier than the natural freezing nuclei can, and in this way it should tend to increase the local precipitation.

The onset of glaciation in cloud tops can be quite easily recognized from the appearance of the cloud itself. Figure 4 shows a cumulus cloud that consists entirely of water droplets and has a sharp, cauliflower-like outline. Figure 5 shows the same cloud after the top has become glaciated, in this case after the introduction of silver iodide particles. The ice crystals are blowing away from the top of the cloud, giving it a characteristic anvil shape and soft outline, while heavy rain can be seen falling from the base. Exactly the same sort of behavior occurs with natural freezing nuclei.

This precipitation process has been investigated from many points of view, but here we are concerned with its very first stages—stages leading up to the production of ice crystals in the required concentration in the cloud top. The three major questions to be answered concern the origin of the natural freezing nuclei that are active at tem-

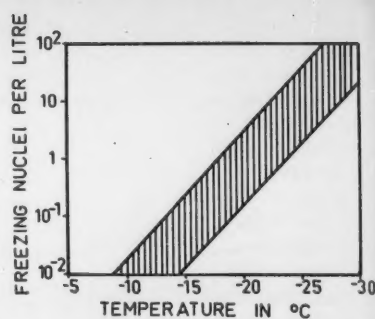


Fig. 2. Average activity distribution for ice-forming nuclei in the atmosphere. The activity curve varies from day to day but typically lies within the shaded region.

peratures above about  $-20^{\circ}\text{C}$ , their chemical composition, and the mechanism by which they cause the production of ice crystals. Each of these questions is still a source of discussion and controversy, but considerable progress appears to have been made toward their solution.

### The Meteor Hypothesis

The meteor hypothesis, put forward by Bowen in 1953, states that at least a substantial fraction of the more active freezing nuclei in the atmosphere have their origin as micrometeoritic particles collected by the earth in its orbit through space. The evidence which leads to this conclusion is of an indirect and statistical nature, as I shall now show.

Rainfall on the earth's surface is influenced by many factors, some of which are periodic (like the seasons) and many of which, on a shorter time scale, are much more random, though there may be serial correlations due to such things as the movement of pressure systems. It is therefore to be expected that when a sufficient number of data from different places and different years are combined to give a single curve for rainfall as a function of day of the year, a smooth curve will result.

The great difficulty lies in estimating the degree of departure from smoothness which is statistically significant when a given number of records have been combined, and of course this also depends in detail on the exact method used to treat the data, since daily rainfall is far from normally distributed. Nevertheless, when Bowen combined the rainfall records for 300 stations widely distributed in both hemispheres

(each station contributed records for a period of about 50 years), the deviations from smoothness were so large that it seemed reasonable to regard them as significant without any detailed statistical analysis.

Bowen's world rainfall curve for the months of November, December, and January is shown in Fig. 6. It can be seen that deviations from the mean are as large as  $\pm 15$  percent and that some peaks, particularly those of 12 and 22 January and of 1 February, are particularly prominent.

Since the publication of this curve, Brier of the U.S. Weather Bureau has carried out an independent analysis of rainfall data from 150 stations distributed over the United States. The choice of the stations and years involved was such that none of the data had been included in Bowen's curve. Using careful statistical techniques Brier showed that there was a high correlation between the dates of rainfall maxima and minima among the two sets of data which he used and the world rainfall curve of Bowen. The probability of the observed level of correlation occurring by chance was estimated to be less than 1 percent.

A less elaborate, but again completely independent, analysis of rainfall

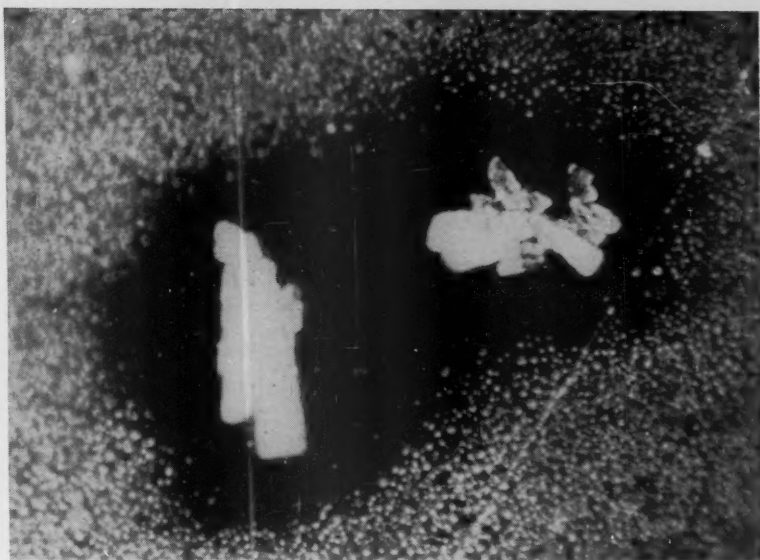


Fig. 3. Two ice crystals growing among a population of water droplets on a microscope slide. The ice crystals shown are about 100 microns in maximum dimension, while the water droplets are typically about 2 microns in diameter.

records, from stations in the U.S.S.R., by Dmitriev and Chili yielded 30 rainfall peaks over the whole year which were considered to be statistically significant. The agreement between the dates of these peaks and those in the

appropriate part of Bowen's curve was again very good.

These studies appear to have established fairly firmly the existence of world-wide, annually recurring singularities in the terrestrial rainfall pattern.

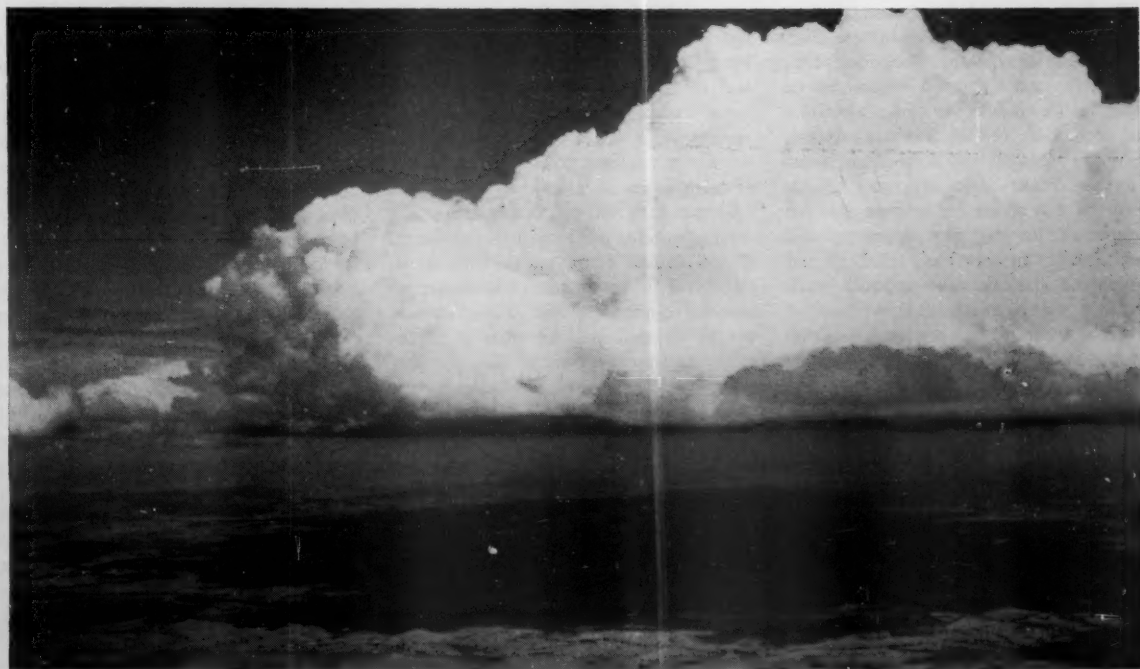


Fig. 4. A cumulus cloud consisting entirely of water droplets. Note the sharp outline and the uniform base level, which shows how definite is the onset of condensation. [Commonwealth Scientific and Industrial Research Organization]





Fig. 5. The cloud shown in Fig. 4 about 30 minutes after seeding with silver iodide smoke. The top of the cloud now contains large ice crystals, which may be seen blowing downwind in a typical "anvil." Heavy rain can be seen falling from the cloud base. [Commonwealth Scientific and Industrial Research Organization]

If then, these rainfall peaks are real, they must be due to some physical phenomenon in the atmosphere, and both the global nature of the singularities and their annual recurrence appear to require some sort of extraterrestrial mechanism. It was for this reason that the meteor hypothesis was put forward.

When a correlation is sought between rainfall peaks and known meteor showers it is natural to expect that the meteor shower will precede the rainfall peak by an appreciable period, during which the meteoric dust settles through the stratosphere and reaches the level of convective mixing below the tropopause. With this in mind, Bowen found a correlation between his rainfall peaks and intense meteor showers occurring about 30 days previously, as shown in Table 1.

More extensive correlations have been found for other parts of the year, both by Bowen and by Dmitriev and Chili, and the correlation has been strengthened by the recognition of periodicities in rainfall peaks associated with periodic meteor showers such as the Perseids in September, the Giacobinids in October, and the Bielids in December. Most recent work has, however, concentrated upon the well-defined peaks

and prominent meteor streams indicated with asterisks in Table 1.

A rather striking feature of the meteor hypothesis is the time lapse of  $30 \pm 2$  days between the meteor shower and the rainfall peak with which it is associated. The most obvious conclusion is that this is the time required for the meteor particles, slowed to terminal velocity at a height of about 80 kilometers, to fall under gravity to the level of the tropopause. If this is so, then it can be estimated that the particles involved must have a diameter of about 10 microns, and the sharpness of the rainfall peak implies a corresponding sharpness in the size distribution. I discuss this aspect of the theory in more detail later.

### Supporting Evidence

Evidence supporting the meteor hypothesis, or at least consistent with it, has come from a variety of sources. In the first place, if the rainfall peaks are real and due to a sudden increase in the freezing-nucleus content of the atmosphere, then it would be helpful to have a direct measurement of this in-

crease. Now the concentration of freezing nuclei in the air can be measured directly by a fairly simple technique. An air sample of known volume is placed in a container, humidified, and cooled down in such a way that a supercooled cloud forms. If any freezing nuclei are present that are active at the temperature of the cloud, they form ice crystals, which grow and fall to the bottom of the container. If the bottom of the container is coated with a supercooled sugar solution, then, on falling into this solution, the tiny ice crystals grow rapidly to visible size and can easily be counted.

Freezing-nucleus counters of this type have, over the last few years, been operated daily during the month of January at a number of stations in Australia, New Zealand, South Africa, Sweden, England, France, Germany, and the United States. January was chosen for this study because the distinct peaks in the rainfall curve for this month led one to hope that the freezing-nucleus count might show a similar simple pattern.

The results of several years' operations have established that the freezing-nucleus count in most places does fluctuate.



tuate greatly from day to day, and that concentration peaks of one or two days' duration frequently occur. The records often vary greatly from station to station; however, when a composite curve is drawn for all stations there appear to be fairly well defined peaks occurring within one or two days of the peaks in the rainfall curve.

More recently Bigg, at the Radiophysics Laboratory, has developed a counter which continuously monitors the freezing-nucleus content of the air around it. This device has established that freezing-nucleus peaks may be of very short duration, rising to a maximum in one or two hours and then decaying more slowly toward the background level. If purely local nucleus sources are ruled out by investigation, then it would appear that such sharp peaks occur after the breakdown of a temperature inversion separating nucleus-poor air in the lower layers from nucleus-rich air above. The occurrence of these rapid fluctuations requires that some sort of integrating technique be used if a representative daily nucleus count is to be taken.

A second study which also has given a measure of support to the general picture is a census of the occurrence of cirrus cloud over wide areas. Cirrus cloud consists of ice crystals formed high in the atmosphere, and a dense cirrus cover may reasonably be associated with either a high concentration of freezing nuclei or a high concentration of water vapor, or both, at that altitude. Bigg, who also carried out this work, examined available records of the occurrence of cirrus cloud over Australia and found maxima in the cirrus cover on or near peak days in the rainfall curve. In a similar study in the United States, however, Braham failed to find any significant correlation between the two curves.

A very important piece of supporting evidence has recently been obtained. It has been known for some time that, within the altitude limits conveniently available to ordinary aircraft, the freezing-nucleus concentration shows no over-all tendency to decrease with height. This finding is rather unexpected if it is supposed that the nuclei originate at the earth's surface, but it is completely in accord with the meteor hypothesis. Now, at an altitude of about 10 kilometers there is a more or less permanent inversion, the tropopause, which should act as a substantial

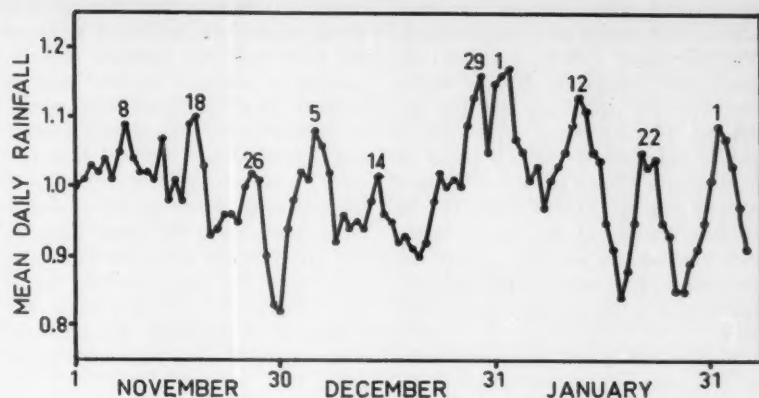


Fig. 6. Bowen's world rainfall curve.

barrier to material of terrestrial origin. In 1959, however, Telford of the Radiophysics Laboratory succeeded in making several measurements of freezing-nucleus concentration above the tropopause and established that the concentration at those altitudes was quite comparable to that below the tropopause.

Towards the end of 1960, using a new sampling technique and with the aid of U.S. Air Force U2 aircraft, Bigg was able to sample freezing nuclei to a height of 20 kilometers. These measurements confirmed those of earlier trials with balloon-borne equipment and again showed high nucleus counts above the tropopause, giving substantial support to the meteor hypothesis.

A related experiment at present being carried out promises to yield additional information about conditions in the high stratosphere. If small meteor particles enter the earth's atmosphere they either fall gently at the appropriate terminal velocity or else burn up during their deceleration. The dividing line between these two types of be-

havior occurs at a particle radius of about 10 microns. The smaller particles are slowed to a low velocity at a height of about 80 kilometers, and at this height their concentration becomes appreciable. The particle concentration at these heights can be studied by examining the light scattered from this layer in the twilight zone, when it is illuminated by the sun and when lower layers of the atmosphere are in shadow. This technique frequently shows pronounced concentrations of particles at this height and may provide valuable information about the number of particles captured from meteor showers, though of course it cannot be inferred that these particles are active as freezing nuclei.

### Criticism of the Theory

Many aspects of the meteor hypothesis and the evidence brought forward to support it have been strongly criticized, and agreement has by no means yet been reached.

Much of the initial criticism questioned the reality of the rainfall peaks from both a physical and a statistical point of view. At this stage the criticism was perhaps justified, since relatively few data had been combined to give the rainfall curve. The curve of Fig. 6, however, representing as it does some 15,000 station-years of measurements, seems adequately representative of the world rainfall pattern.

The associated statistical question relates to the significance of the "peaks" in Fig. 6 and is much more difficult to answer in view of the weighting and smoothing procedures used to obtain

Table 1. Correlation between rainfall peaks and meteor showers.

Rainfall peak (date)	Meteor shower		Time lapse (days)
	Meteor stream	Date	
8 Nov.	Giacobinids	9 Oct.	30
18 Nov.	Orionids	20-23 Oct.	29
26 Nov.	?		
5 Dec.	Taurids	3-10 Nov.	32
14 Dec.	Leonids	16 Nov.	28
29 Dec.	Bielids I	27 Nov.-15 Dec.	—
1 Jan.*	Bielids II	2 Dec.	30
12 Jan.*	Geminids	13 Dec.	30
22 Jan.*	Ursids	22 Dec.	31
1 Feb.*	Quadrantids	3 Jan.	29

\* Well-defined peaks.

the rainfall curve, and of the non-normal distribution of rainfall records. The later work of Brier has, however, given very convincing support to the view that the peaks are real and significant. It would be of great value if similar independent analyses could be made of the almost countless alternate sets of rainfall records kept by the weather bureaus of the world. When such analyses are available, expert statisticians will be able to determine the significance of the correlations between them.

Perhaps the more interesting areas of disagreement concern physical aspects of the theory. For the meteor hypothesis to be regarded as vindicated, the following points must be estab-

lished: (i) that meteor particles can act as efficient freezing nuclei at cloud-top level; (ii) that sufficient meteoric material is collected by the earth to account for a significant proportion of the observed freezing-nucleus population active above  $-20^{\circ}\text{C}$ ; (iii) that there is no terrestrial source of such freezing nuclei which greatly outweighs the contribution of the meteor particles; and (iv) that the arrival of the meteor particles at the earth's surface (or at the tropopause) as a sharp pulse after a delay of  $30 \pm 2$  days is a necessary consequence of some reasonable mechanism.

None of these points has yet been conclusively proved or disproved, and it is in their investigation that most in-

terest lies at the present time. Let us consider them in turn.

The theory of the action of solid particles as ice-forming nuclei is as yet in the early stages of its development. Enough is known, however, to suggest that an efficient ice-forming nucleus should be of the order of 0.1 micron in diameter, or larger, and that it should consist of some more or less polar compound whose atoms are so arranged that crystal faces, when exposed, can match fairly closely the molecular arrangement on some low-index face of ice. This is illustrated for the case of two of the most efficient nucleating substances known—silver iodide and lead iodide—in Fig. 7.

Now, meteoric particles may be either metallic or stony in nature. If metallic, they consist predominantly of an iron nickel alloy which seems most unlikely, on theoretical grounds and on the basis of laboratory tests, to have any appreciable activity as an ice nucleus. This conclusion, however, neglects an important possibility, and that is that small metallic particles may undergo chemical reactions as they fall through the atmosphere and may become coated with some ferrous salt which is itself a good nucleating agent. The situation is somewhat similar for stony meteoric particles. Powders or vapors made from stony meteorites have little activity in the laboratory, but it is not known to what extent such meteorites are typical in composition of the micrometeorites in which we are interested, or to what extent abrasion or vaporization duplicate the influences to which the micrometeorites are subjected. The question of the activity of meteoric particles thus still remains open.

Estimates of the amount of meteoritic material accreted by the earth are necessarily indirect and differ from each other by as much as six orders of magnitude, so to evaluate the sufficiency of meteors as a source of nuclei is almost impossible. Evidence from examining snowflakes and from using a particle-size discrimination counter on Bigg's continuous nucleus counter suggests that most active freezing nuclei in the atmosphere are of the order of 1 micron in diameter. If this is true, then most of the estimated meteor accretion rates are somewhat too low to account for the observed nucleus concentration, but the higher estimates of some workers and the general uncertainty leave this question open.

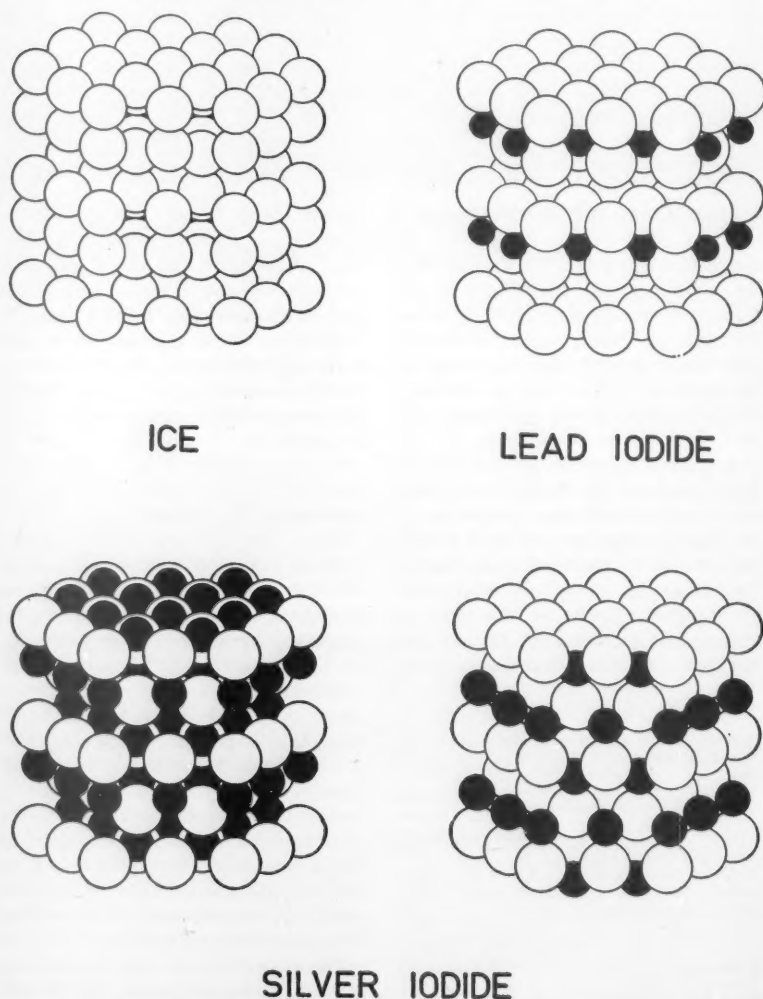


Fig. 7. Molecular models, all to the same scale, of small crystals of ice, lead iodide, and silver iodide. In ice, only the oxygen atoms are shown; in the other two crystals the white spheres represent iodide ions; the black spheres represent the metallic ions.

A related question concerns the relative accretion rates of shower and sporadic meteorites. If the fluctuations in daily freezing-nucleus counts are taken to be caused by fluctuations in the meteoritic accretion rate, then one would expect that the accretion rate during showers would be as much as 100 times the sporadic accretion rate. The weight of evidence at present available suggests that this is not so, and that despite the considerable increase in visible meteors during showers, the total accretion rate changes relatively little. Present meteor-counting techniques, however, are limited to particles rather larger than those we have been considering, and it is possible that meteor streams may contain rather large numbers of these submicron particles.

When the possibility of a terrestrial source of freezing nuclei is examined, data are much more easily found. Mason and his co-workers in England have examined the ice-nucleating properties of many naturally occurring minerals and have found at least one, kaolinite, which is apparently sufficiently common and active to account for all observed nuclei, and at the same time not so abundant as to cause a saturation of the air with its particles.

A criticism which may be made of these experiments is that we cannot be sure that the freshly ground mineral samples tested are typical in activity of the particles of this same mineral which might find their way into the atmosphere through processes of erosion. In fact it has been shown that the nucleation activity of many mica-like materials decays very rapidly on exposure to humid atmosphere conditions, and this may well occur with other minerals too.

The suggested activity of kaolinite is, however, supported by Japanese work in which the nuclei at the centers of snow crystals were examined by electron diffraction. The particles were, in most cases, several microns in diameter,

and the diffraction pattern suggested a clay mineral of the general type of kaolinite.

Industrial processes, particularly those associated with ore smelting, which have been found to liberate vast quantities of active nuclei, are another possible source of freezing nuclei on the earth's surface.

Against this must be set, however, the fact that active nuclei are found in apparently undiminished concentration over the Southern Ocean, a thousand miles from any possible continental source, and high above the tropopause, where particles originating at the earth's surface would not be expected to penetrate. Our knowledge of the fate of tiny particles injected into the atmosphere is, however, not sufficiently exact at present for any firm conclusion to be drawn.

Finally, we consider the requirement that the meteoric nuclei arrive with a well-defined front at the tropopause after a delay of  $30 \pm 2$  days. The only mechanism which has been suggested for this effect is the free fall of the particles at their terminal velocities through the stratosphere. Rough calculations of this process suggest that a 30-day fall time should be associated with particles about 10 microns in diameter. This accords well with the maximum size for a meteor particle that remains unmelted in its fall, and also with the general size of particles found in snowflakes and cirrus crystals. These particles do not, however, show any sharp size preference, and indeed the majority of nuclei measured at the earth's surface are less than 1 micron in diameter.

Again, it is hard to see why the "peak" should remain sharp after 30 days, since this would require an almost unbelievable uniformity of particle size, and no such uniformity is evident at the earth's surface. It seems that if the meteor hypothesis is valid there must be some as yet undiscovered mech-

anism which either limits the size range of efficient nuclei or else transports all nuclei through the stratosphere by some mechanism other than simple falling. Until such a mechanism is suggested, this will remain one of the most serious obstacles to any general acceptance of the meteor hypothesis.

## Conclusion

During the past eight years the meteor hypothesis has provided a stimulus for much interesting and valuable work on the origin and properties of natural freezing nuclei in the atmosphere. In many ways the results of this work appear to support the hypothesis, but several steps of rather crucial importance to the argument are still unexplained, and other groups of experiments point towards a terrestrial origin for the nuclei.

It is still too early to decide which view is correct. If, however, as appears to be the case, the rainfall singularities are real, then the meteor hypothesis is the only one which has been advanced as yet which seems capable of explaining them.

## Note

1. To call these particles "freezing nuclei" implies that they act by causing the freezing of a water droplet. Another possibility is that ice may form directly upon the foreign particles by sublimation from the vapor, in which case they should be termed "sublimation nuclei." Particles are known which act in both these ways, and what happens depends in detail upon temperature and humidity. For this reason the inclusive term *ice-forming nuclei* is perhaps to be preferred, but tradition has established the use of *freezing nuclei*, and I follow it here.

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# Genes and the Pigment Cells of Mammals

Pigment cells provide unique material for studying the interactions of genetic determinants.

Willys K. Silvers

Interest in the genetic aspects of mammalian pigmentation is almost as old as the science of genetics itself, for it was only shortly after the rebirth of Mendelism, at the beginning of this century, that W. E. Castle and his students, at the former Bussey Institute of Harvard University, initiated studies on the inheritance of specific coat-color types in guinea pigs, rats, rabbits, and mice. Although these workers were completely unaware of the anatomical basis and biochemistry of pigmentation, the genetic analyses resulting from their extensive breeding studies established that the production of coat-color pigment patterns involved a local interaction of specific gene products which was relatively unaffected by systemic or environmental factors. It remained for subsequent investigators to produce experimental evidence confirming the belief of some of the older histologists that melanogenesis is the sole prerogative of specialized branched or dendritic cells, now usually referred to as melanocytes, of neural-crest origin, which function as unicellular melanin-secreting glands in the epidermis (1). This elucidation of the cellular basis of pigment formation, made a little more than two decades ago, set the stage for extensive studies on the physiological genetics of pigmentation. These are directed toward answering the important question of how the genes which influence pigmentation produce their effects, and it is this that forms the principal subject matter of this article.

The genetic aspects of mammalian pigmentation have been more thor-

oughly worked out in the mouse than in any other species, for two reasons. Large numbers of coat-color mutations—that is, deviations from “wild type”—have occurred in this species (2), and the requisite stocks manifesting these mutations either are available or can be produced comparatively easily because of the large number of inbred strains in existence. Although most of what follows, therefore, concerns studies on the mouse, it may be emphasized that the general principles illustrated certainly apply with relatively few qualifications to other mammals.

## Recognition of Genes Concerned with Pigment Formation

Since the effect or effects of a particular genetic locus can only be established on the basis of variations (alleles) from the “wild type” that have been produced by mutations, it is obvious that the whole field of physiological genetics of pigment patterns has depended entirely upon the occurrence, recognition, and description of mutations, along with their preservation. For example, the so-called wild-type coat color in mice is probably best described as “grey-bellied agouti.” Animals of this color have a yellow banding of the otherwise black hair on the dorsum and a yellow terminal ticking of the ventral pelage. It is evident, however, that if mice of only this one phenotype were available for pigment studies, very little, if anything, could be found out about the number and action of specific genes which are responsible for producing this pigment pattern. An understanding of the genetic factors

concerned has been made possible by the occurrence of deviant coat-color types produced by gene mutations. The investigation of the individual effects of these mutations reveals which aspect of melanogenesis is controlled by the so-called wild-type allele.

It is obvious, therefore, that in the mouse there must still be a very large number of gene loci, in some way involved in pigment formation, about which we know nothing at present and about which we may learn something in the future only if mutations appear. Nevertheless, enough coat-color mutations have occurred in this species to make a systematic analysis of their effects one of the most fruitful means of exploring the many diverse ways in which gene action and gene interaction can influence the distribution, morphology, synthetic activity, and so on, of a single cell—the melanocyte.

## Studies on Pigment Granules

Although casual examination of murine hair shafts might suggest either that the pigment is in the form of a solid mass or that it is homogeneously distributed, careful microscopic study reveals that the color of hairs results principally from the presence of very tightly packed clusters of pigment granules. When hairs are actively growing, the half-dozen or so melanocytes in the generative region of their follicles are continuously supplying pigment granules to the adjacent Malpighian cells of the upper bulb, which are to form the medulla and cortex of the hair shaft. There seems to be a direct transfer of the melanin which the melanocyte secretes, by way of the end processes of the cell's branches, into the cytoplasm of these neighboring cells (see Fig. 1). This apparently unique direct transfer of the secretory product of one cell into the cytoplasm of another has been aptly described by Masson (3) as “cytotrine” activity.

Since pigment granules are the basic unit of pigmentation, all coat-color mutations, except those that produce white spotting, must necessarily produce their effect by altering in some way the various attributes of these granules. This became evident from the results of E. S. Russell's systematic histological investigation of the pigment of the hair shafts in different inbred color stocks of mice (4). Probably the most surprising outcome of

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this study was that, in spite of all the different color hues to be seen in the coats of mice, only two basic kinds of pigment granules were found—oval or spherical black and brown granules, which are classified as eumelanin, and the much smaller, round, yellow granules known as pheomelanin.

In the light of recent work (5) it appears almost certain that both these melanins are protein conjugates. Eumelanin is formed by the coupling of a quinonoid polymer, indole-5,6-quinone, with protein. The polymerization and coupling processes occur on the surface of the subcellular cytoplasmic granule—the anlage of the mature pigment granule. The quinonoid polymer is derived from the amino acid tyrosine, by a chemical reaction catalyzed by the copper-containing enzyme tyrosinase, which is attached to the granule. Not very much is known about the synthesis of pheomelanin, although it appears that tyrosine is also involved in its formation. In the hair-bulb melanocytes of mice, the so-called *A* or agouti locus determines which of these types of melanin granule will be produced.

Although the nature (eumelanin or pheomelanin) of the melanin granules which occur in the hair shaft is extremely important in determining the coat-color phenotype, other genetically determined attributes of the melanin granules, such as their size, shape, and color density, also play important roles. Marked differences in coat coloration can also be traced to the influence of certain genes on the number of granules, as well as to the distribution of the granules in the hair shafts. There is no correlation in some of the attributes of pigment granules. For example, the nature, degree of granular clumping, and amount of pigmentation are determined independently; other attributes, such as the nature of granule color and the extent of variation in granule size, are interrelated.

From such comparative studies on the distribution and qualities of pigment granules in hairs, the roles of some of the major genes concerned with pigment formation in the mouse have been deduced. For example, it was concluded that the principal effect of substituting the mutant genes *bb* (brown) for *B*- (black) at the so-called *B* locus involved a qualitative change which implicated only the formation of eumelanin, having no appreciable effect on pheomelanin synthesis. The four allelic

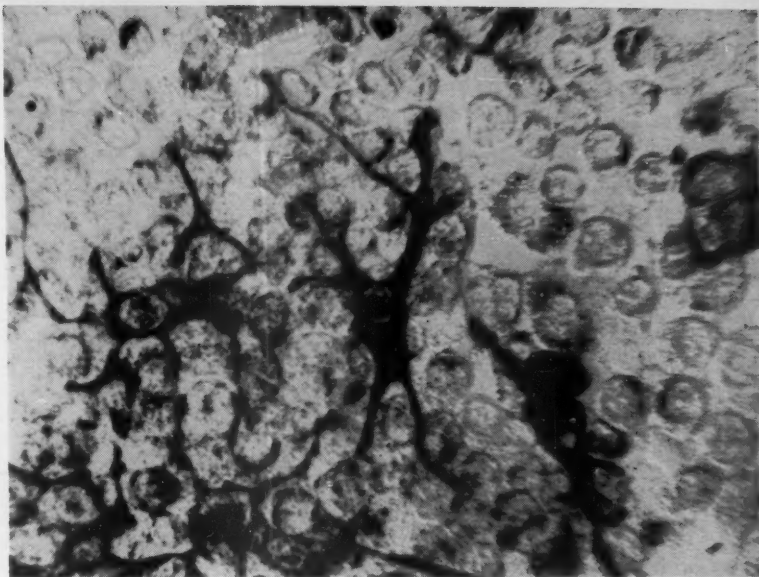


Fig. 1. Living melanocytes in a squashed preparation of epidermal cells prepared from the black ear skin of a guinea pig. Notice the characteristic branches originating from the perikaryon of the melanocytes and the characteristic end caps terminating the end processes. These end caps are applied to the cytoplasm of cells of the Malpighian series. (About  $\times 500$ )

genes at the albino locus (*C*, *c<sup>ch</sup>*, *c<sup>+</sup>*, and *c*) appeared to control in a purely quantitative manner the general level or intensity of pigmentation without affecting its nature. This suggested that this locus controlled the formation or availability of some substance, now known to be the enzyme tyrosinase, essential for the formation of all pigment. Substitution of *pp* (pink-eyed dilution) for *P*- (intense or wild type) altered both the size and the shape of the pigment granules and also reduced the level of pigmentation. Finally, the main effect of incorporating either *dd* (dilute) or *lnln* (leaden) genes into an otherwise wild-type genetic background was to alter the pattern of the deposition of pigment granules in the cells of the hair shaft: the granules formed large granular clumps, unevenly distributed among the septules, instead of being distributed in a more orderly pattern.

Current electron-microscope studies by Frank Moyer of Johns Hopkins University (6) may help to localize the primary effects of some of these loci on the fine structure of melanin granules. Moyer is working on the retinal pigment granules of embryonic and neonatal mice derived from the same color stocks that Russell used. Some interesting findings have already

been disclosed. For example, Russell's observations that the melanin granules of *pp* mice are irregular in shape and smaller than those of the wild type has been shown to stem from an early difference between *pp* and *P*- animals in the formation of the pigment granule, the internal fibers of *pp* granules differing in their order of arrangement from those of the wild type. Furthermore, it has been shown that in the albino mouse (*cc*), although mature melanin granules are not formed, unpigmented "precursor granules" similar in appearance to granules of the corresponding developmental stage in the wild type do exist. It seems likely, therefore, that tyrosinase activity is blocked at this stage.

Further studies along these lines may even reveal the existence of subtle changes in the granules of animals heterozygous for some color factors that we regard at the moment as completely recessive.

#### Enzymatic Studies

Not only have detailed investigations been made of the pigment granules of coat-color mutants but considerable attention has also been devoted to the capacity of hair bulbs, or even of skin

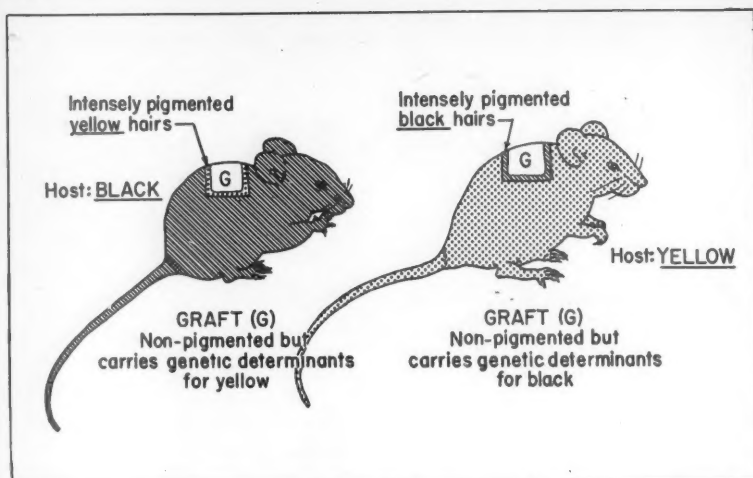


Fig. 2. Intensely pigmented black and yellow mice, grafted at birth with histocompatible skin from newborn genetically yellow (but nonpigmented) and genetically black (but nonpigmented) mice, respectively, exhibit some intensely pigmented hairs within the graft margin when grown. These hairs are pigmented by host melanocytes which have migrated into hair bulbs of the graft, where their functional behavior is dictated by the milieu (agouti-locus genotype) of the graft.

extracts, of various genotypes to bring about the oxidative blackening of 3,4-dihydroxyphenylalanine (dopa), now known to be an intermediate product in the synthetic pathway that leads to synthesis of melanin. One interesting conclusion from these studies, principally carried out by Sewall Wright and his students (7), is that the intensity of the dopa reaction (the darkening of the extraction mixture when extracts are employed, or darkening of the cytoplasm of melanocytes when frozen sections are used) parallels very closely the intensity of the yellow pigmentation of the skin under study. In black and brown genotypes the intensity of the dark pigment produced corresponds with the amount of yellow that would have been produced if the animals had been genetically yellow.

Similarly designed experiments, in which tyrosine and tryptophane were used as substrates, have been carried out by Morris Foster of the University of Michigan (8). These suggest that tryptophane or one of its metabolites may be a precursor of pheomelanin.

#### Sites of Gene Action in Pigment Patterns

Although the work just outlined has contributed greatly to our understanding of the way in which genes involved in pigmentation produce their

effects (and there is certainly scope for further studies of this type), its shortcoming lies in its failure to reveal whether the specific effects which different genes have on the pigment granule are mediated through the melanocyte itself or whether these effects reflect a primary action on the part of the environment in which this cell occurs.

To illustrate this point let us return to the wild-type mouse and the agouti pattern which characterizes it, a pattern which involves the elaboration of both black and yellow pigment in the same hair, and which is determined by the *A* locus. Five different mutations have now been described at this locus, and when these various mutants are incorporated into an otherwise wild-type genetic constitution, phenotypes are produced which vary from animals that are all black (extreme nonagouti, *a<sup>a</sup>*) and animals that are all yellow (*A<sup>+</sup>*) to animals that have a black dorsum and a yellowish ventrum (black-and-tan, *a<sup>t</sup>*). Although this shows that the series of alleles at the *A* locus determines the nature of the melanin produced by the melanocytes of the hair bulb (that is, determines whether it is eumelanin, pheomelanin, or both), it does not indicate whether the alleles at this locus produce their effect by acting autonomously within the hair-bulb melanocytes themselves or by acting indirectly in conditioning the

follicular environment in some manner which, in turn, affects the behavior of the melanocyte. These alternatives are important, since the former indicates that each agouti-series genotype differs from the others at the level of its melanocytes, whereas the latter alternative implies a similarity in melanocytes but a difference in tissue environments.

Determination of the primary site of action of the genes at the *A* locus requires a study of the behavior of melanocytes of one agouti-locus genotype experimentally incorporated into developing hair follicles composed of cells of a different agouti-locus constitution. This experimental condition can be achieved by transplanting compatible grafts of ventral or dorsal skin between newborn mice differing with respect to the nature (the agouti-locus constitution) and intensity (governed by other loci) of their future pigmentation. It takes advantage of the fact that some host melanocytes migrate across the graft boundary and establish themselves in developing follicles of the alien genotype (see Fig. 2). A difference in intensity of pigmentation between host and graft is of course essential in order that hairs of the graft which are pigmented by host melanocytes can be recognized.

It has been found that the agouti-locus genotype of the graft always determines whether eumelanin, pheomelanin, or both are produced by the "foreign" pigment cells of host origin (9). Thus, when potentially black melanocytes migrate into dorsal or ventral hair bulbs which, although phenotypically nonpigmented, are genetically yellow, intensely pigmented yellow hairs are produced (Fig. 2). When similar melanocytes are introduced into agouti (but nonpigmented) hair bulbs, the typical wild-type or agouti hair pattern results. Additional findings suggest that this expression of genic activity is dependent not only upon the genotype of the follicular environment but also upon the location of this environment on the integument. For example, when either genotypically yellow or genotypically black pigment cells invade a dorsal, nonpigmented, black-and-tan graft they produce intensely pigmented black hairs, whereas when they are incorporated into ventral follicles of the same genotype, yellow hairs with black bases (characteristic of the ventral hairs of intensely pigmented black-and-tan mice) result. This finding, in

conjunction with the observation that black-and-tan melanocytes are also able to respond completely to the agouti-locus genotype of the receiving hair follicle, implies that, in black-and-tan mice, ventrality and dorsality of location are not important *per se* but that, together with their genetic constitution, they present different follicular environments which influence the expression of the melanocyte.

The importance of the hair follicle in promoting the elaboration of pheomelanin is also emphasized by the fact that in yellow mice it is only in the hair follicle that pheomelanin is produced. In all parts of the animal where extrafollicular melanocytes are found—for example, the ear skin, tail skin, or eye—only eumelanin is synthesized (10). It is therefore evident that the inherent capacity of melanocytes of all genotypes is to produce eumelanin, but that in the local milieu of “physiologically” appropriate hair bulbs they produce pheomelanin. The exact part played by the alleles at the *A* locus in promoting this physiologically appropriate environment still remains to be determined. When this has been determined we will be one step closer to understanding the primary gene action of these alleles.

The experimental design described above has also served in investigating whether other loci involved in melanin formation in the mouse act within the melanocyte or act through the neighboring cells of the Malpighian system composing the environment. For example, in the agouti-locus study it was found that the *C*-locus genotype of the receiving hair follicle had no influence on the immigrant melanocytes of host origin, the intense pigmentation of the host (*C*-) expressing itself in the genotypically albino (*cc*) or lightly pigmented (*c<sup>c</sup>c<sup>c</sup>*) hair bulbs of the graft. This locus, therefore, apparently acts autonomously within the melanocyte. Similar studies involving host-donor combinations which differed at the *B* and *P* loci also indicate that these loci act within the pigment cell.

It has already been mentioned that the main effect of both *dd* (dilute) and *lnln* (leaden) genes on the granules of the hair is to cause the formation of large, unevenly distributed granular clumps, which are responsible for the lighter appearance of these genotypes. In other investigations the origin of this clumping effect has been

traced to a difference in the morphology of *dd* and *lnln* melanocytes as compared with melanocytes of the wild type (*DDLnLn*) (10) (see Fig. 3). Whereas the melanocytes of wild-type animals are characterized by the possession of long, relatively thick dendritic processes, in *lnln* and *dd* animals the pigment cells have fewer and finer dendrites. Because of this altered morphology, melanin granules are largely clumped around the nucleus in the body of the cell. Since the dendrites are the channels through which the granules are secreted, the reduction in size and number of the processes in *dd* and *lnln* mice may interfere with the transfer of pigment granules to the epidermal cells; this interference could account for the irregular distribution of the granules in the hair shafts of these mice.

To determine the site of action of

the genes at these loci, Clement L. Markert and I (11) transplanted embryonic tissues containing potential melanocytes (melanoblasts) from normal, leaden, and dilute animals into the anterior chambers of the eyes of adult albino or pink-eyed mice having the same or different *Ln* and *D* constitution as the graft. The results were consistent with the hypothesis that, although the genes at both the *D* and *Ln* loci exert their activity from within the developing melanoblast, the number and size of dendritic extensions of a pigment cell is probably another function of the environment in which the cell resides. Melanocytes of *dd* and *lnln* genotypes have an innately weak capacity for extending dendrites, as reflected by their altered morphology in the rather compact tissue environments where they normally occur. However, in the less restrictive tissue

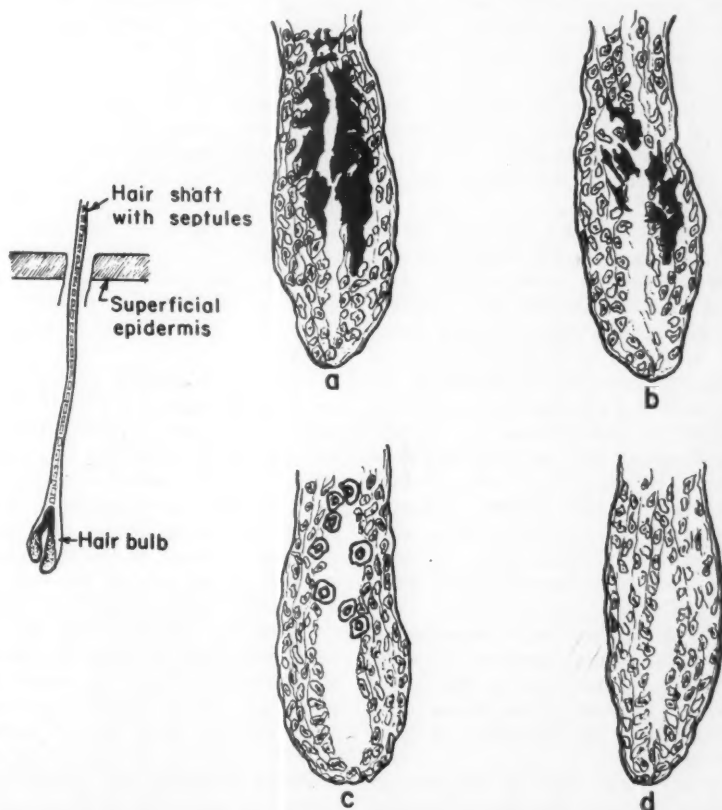


Fig. 3. Hair-bulb regions of follicles of different genotypes, illustrating differences in their melanocyte components. In the wild type (a) the many dendritic processes of the melanocytes of the bulb almost completely obscure the matrix, whereas in *dd* and *lnln* genotypes (b) the clumped arrangement of melanin granules around the nucleus of the cell makes it possible to identify individual pigment cells. The albino, or *cc*, genotype is characterized by the occurrence of large clear cells (c), which have been shown to be amelanotic melanocytes. These cells do not occur in hair bulbs originating in white spots (d).



environments in the eye, *dd* and *lnln* melanocytes do extend more and longer dendritic processes and in many instances are indistinguishable from the melanocytes of the wild type. Thus it appears that the *Ln* and *D* genotype of the pigment cell is expressed distinctly only in suitably compact tissue environments.

### Genetic Factors in Melanoblast Differentiation

So far I have attempted to describe some of the experimental methods used to determine how certain loci, known to be involved in the formation of the pigment granule and its deposition into the growing hair, produce their effect. These methods have revealed that some of these loci act autonomously within the melanocyte, regardless of the tissue environment in which the melanocyte occurs; others exert their activity from within the developing melanoblast but produce their effect only in a suitable tissue environment; and still others produce their effect by altering in some way a particular tissue environment which, in turn, affects the behavior of the pigment cell.

The fact remains, however, that in all these cases we are dealing only with various ways in which specific genes can affect the product of a differentiated cell—the pigment granule. There is, in addition, a whole series of gene loci which, instead of influencing the product of the melanocyte, exert their effect on pigmentation at a more fundamental level by controlling some aspect of melanoblast differentiation. Probably the best examples of genetic factors in this category are those associated with white spotting—a character which is widespread among mammalian groups.

As background for a discussion of the physiological genetics of white spotting, I shall give a brief introductory account of the origin, early embryology, and occurrence of melanocytes.

The neural crest of the embryo, which originates between the junction of the neural tube and its overlying ectoderm, besides forming melanocytes, gives rise to cells which form the dorsal root ganglia of the spinal nerves, the adrenal medulla and other chromaffin tissue, and the Schwann cells of all peripheral nerves. Initially the

neural crest is continuous from front to back, but as development proceeds its constituent cells migrate ventrolaterally on either side of the spinal cord and at the same time become segmentally clustered. In the mouse, this anterior-to-posterior and mediolateral migration of neural-crest cells from their place of origin to their definitive positions takes place during the 8th to 12th day of embryonic development (the gestation period of the mouse is about 21 days), as demonstrated in the classic experiments of Rawles (12).

In addition to the melanocytes finally located in the basal layer of the superficial epidermis that are responsible for skin pigmentation, and those in the hair bulbs that are responsible for hair pigmentation, there are other melanocytes responsible for the pigmentation of the choroid and iris (retinal pigment cells have a different embryological origin, coming from the outer wall of the optic cup). Melanocytes may also be found in the leptomeninges and in other regions of the brain; they occur in at least some areas of the dermis in nearly all mammals, including man. Indeed, melanocytes have been observed in the parathyroid, the thymus, the ovary, the submucosal connective tissue of the uterus, the sheaths of the tubules of the epididymus, the spleen, the adrenal medulla, and the regional lymph nodes, as well as in many other locations in some species, especially rodents (1).

Whereas the absence of pigmentation in albino animals apparently stems from an inherited metabolic defect in the synthesis of tyrosinase in melanocytes which are normal in respect to their numbers and distribution, it is obvious that white spotting must have a different etiology, inasmuch as some, at least, of the cells of the body in white-spotted animals have the ability to synthesize melanin. This became even more apparent from the results of histological studies in which the white skin of the albino was compared with the white skin of piebald animals (13). In all species so far investigated—mouse, rat, guinea pig, rabbit—the hair bulbs of white-spotted areas are characterized by matrices consisting of regularly arranged cells of equal size, but albino hair follicles contain, in addition, many large “clear” cells in their upper bulb region (see Fig. 3). These large cells with an apparently hyaline cytoplasm are un-

questionably amelanotic melanocytes (melanocytes which are in every respect normal except for their ability to synthesize melanin); there is much anatomical evidence consistent with this interpretation, and in the mouse these cells have been shown to be of neural-crest origin (14).

The matrices of hair follicles arising in white-spotted areas are indistinguishable from those of follicles of artificially whitened hairs produced by x-irradiating pigmented skin with dosages known to cause permanent destruction of the melanocytes of the hair bulb (15), and indistinguishable from hair follicles which develop in skin experimentally deprived of neural-crest derivatives (14). These observations suggest that the piebald condition results either from a complete absence of melanoblasts in affected areas or from the failure of melanoblasts to differentiate locally. Moreover, since there are so many loci associated with white spotting—more than 14 in the mouse alone—it seems reasonable to suppose that both these hypotheses are valid, according to the loci involved, and that either of the mechanisms may be accounted for in a number of different ways. For example, an absence of melanoblasts could be attributed (i) to a genetic disturbance in the neural-crest region specifically affecting the differentiation of neural-crest cells into melanoblasts; (ii) to a genetic effect on melanoblast migration, or to a general metabolic disturbance which occurred during melanoblast migration, so that these cells did not reach all areas of the epidermis; or (iii) to a failure of melanoblasts to survive in the “spotted environment.” A failure of melanoblast differentiation might result either from a genetic suppression within the melanoblasts themselves or from a genetic effect which was expressed only in certain areas of the epidermis. This last possibility is somewhat analogous to the situation in the black-and-tan mouse, where the hair bulbs in different regions of the integument promote the synthesis of different kinds of melanin.

In mice there are some genes—for example, *W*, *W*<sup>+</sup>, *W*<sup>+</sup> (“dominant spotting”), and *Mi*<sup>wh</sup> (“dominant white”)—which, when heterozygous, produce white spotting but when homozygous produce animals which are completely white except for retinal pigmentation. Examination of the skins of these animals has shown them to be essentially



"one big spot," since their hair follicles do not possess any demonstrable amelanotic melanocytes. To determine why these mice are nonpigmented, Markert and I transplanted embryonic tissue containing neural crest from animals destined to be completely white (that is, "one big spot") into an environment that is known to be favorable for melanoblast differentiation and melanin synthesis—the anterior chamber of the eye. Our reason was this: if in such an environment the explants did produce melanocytes, the inability to form pigment in the homozygous mutant could be attributed to action of the environment. In no instance were any pigment cells ever obtained from these grafts (16). These results tend to corroborate the hypothesis that the deficiency in the nonpigmented genotypes lies in the failure of the neural crest to give rise to cells capable of becoming melanocytes.

While this hypothesis seems to explain the complete absence of melanocytes in animals homozygous for these particular mutations, it is insufficient as an explanation of the localized, well-defined white-spotted areas, usually limited to the belly, of animals heterozygous for these same factors. Assuming that an autonomous effect within the melanoblasts themselves is responsible for the all-white condition of, for example, *WW* mice, and that one dose of *W* (*Ww*) genes interfered with the differentiation of some melanoblasts, one might anticipate that the heterozygous condition would result in a "silvering" pattern where pigmented, partially pigmented, and nonpigmented hairs were intermingled, rather than in the localized white spot which occurs. The mutation known as "splotch" in the mouse is pertinent here. Animals heterozygous for this mutation (*Spsp*) have a white belly spot and white extremities, while the homozygote (*SpSp*) dies in utero at approximately the 14th day of gestation, with abnormalities occurring in regions of the neural tube and the neural crest and their derivatives. Robert Auerbach, who studied this mutant (17) by implanting presumptive neural crest of *SpSp*

embryos into the coelom of chick embryos, found that these grafts yielded no pigment, although corresponding grafts from heterozygotes did. The "splotch syndrome" is evidently caused by a disturbance of the region of the developing embryo which includes the neural crest. It therefore appears that although there is little doubt that the primary effect of the *Sp* gene in the homozygous condition is on the neural crest, animals heterozygous for this factor still exhibit localized white spotting.

It is obvious that white spotting still remains one of the most fascinating problems for those interested in gene action and gene interaction. Before leaving this subject I will mention just a few of the many other observations concerned with white spotting that await explanation. Individual mice heterozygous for two loci each of which is involved in white spotting lack pigment in more areas than one would expect merely on the basis of the sum total of the individual effects of each heterozygote. This synergistic effect may produce phenotypes which are almost completely white. Moreover, the amount of white spotting is much greater on a black background than on a co-isogenic yellow background (18). In the guinea pig, the tortoise-shell (*e<sup>h</sup>e<sup>h</sup>*) pattern, characterized by an irregular intermingling of yellow with black hairs, is greatly affected by the presence of spotting factors. Not only is there an increase in the amount of yellow in tortoise-shell genotypes but, in addition, there is a tendency toward segregation of yellow and black so that a tricolored yellow, black, and white phenotype results (19).

## Conclusions

In order to exemplify the many diverse ways in which gene action can influence or suppress pigment production, I have been mainly concerned in this discussion with analyzing how a few well-studied coat-color factors of the mouse produce their phenotypic effect. This analysis demonstrates

that melanoblast differentiation and melanin synthesis proceed through an orderly sequence of genetically controlled steps, any one of which can be influenced in various ways. While some coat-color genes are involved in early steps in melanoblast differentiation (*W*, *Mi<sup>h</sup>*, *Sp*), melanocyte morphology (*D*, *Ln*), or the basic protein structure of the melanin granule (*P*), others produce their effect by controlling tyrosinase synthesis (*C*) or the polymerization of melanin (*A*, *B*). Although much work still remains to be done in tracing the phenotypic effects of these specific loci even farther back, to the time and place of their primary action, these studies have already contributed much to an understanding of how gene action and gene interaction can influence a single mammalian character (20).

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## Science and the News

### The Budget Process: It Changes, Slowly, To Meet New Needs

The controversy over long-term financing of foreign aid has been dominating Congressional debates this week, but the general problem of how to plan and finance programs running over a period of years has also been getting attention, including the question of planning for research and development. The central problem is how the executive branch should plan effectively for long-term programs, a complicated business in itself, further complicated by the budget process, under which the executive departments normally get appropriations from Congress only for a year at a time. The budget process raises two kinds of difficulties: it tends to concentrate the attention of the budget makers on preparing the next 1-year budget for submission to Congress when sound decisions on including an item in the 1-year budget can only be made upon consideration of the long-term implications of the item, for which there is no place in the present budget; secondly, in theory at least, the difficulty is further complicated because, even if the departments have done long-term planning, there is no guarantee that in the future years Congress will supply the money needed to fulfill the plan, even though the decision to spend the first year's money often makes sense only on the assumption that the future money will be appropriated year by year. A third kind of problem also comes up, one which applies especially to scientific programs, which is the problem of fitting a program which draws on the resources of more than one department into the neatly compartmentalized federal budget.

The Defense Department, in response to the first need, has now installed a new system of budget preparation, which will be used in preparing next year's budget, and the system is intriguing, since in addition to requiring the preparation of a 5-year budget, the new system amounts to a back-door ap-

proach to the long-talked-about reorganization of the Defense Department. The 5-year projections will be for the internal use of the Defense Department; the budget presented to Congress will appear in its usual form, which cannot be changed without special legislation, although the 5-year projections will presumably be made available to the Congressional appropriations committees. In addition to making a determined effort to take into account the long-range implications of programs, the new budget system cuts across both the service divisions and the conventional budget categories (research and development, procurement, manpower, etc.). The budget will be developed out of estimates that group together all expenses by function: all costs, for instance, related to the nuclear deterrent force will be grouped together: the Navy's Polaris system, then, would be considered in the same package with the Air Force Strategic Air Command, as would the costs of new weapons systems, for any service, so long as it was part of the nuclear deterrent. Proponents of new weapons systems would have to supply estimates not only of the money needed over the years for research and development on the weapon, but of what it will cost to buy the weapon once it is developed, and what it will cost to maintain the weapon once it is bought. All of this can then be compared with the costs of alternative proposals for strengthening the deterrent force and with the cost of already existing weapons in the deterrent force. In a general way such over-all planning has always had to be done, but the hope is that the new system, by making the planning process more explicit, will lead to wiser decision making: for if all the figures are not brought together in a way that makes clear the choices that have to be made, the whole process becomes fuzzy and it is hard to put responsibility on anyone for making, and being prepared to defend, precise recommendations in terms of the over-all spending.

The problem has a special relation to planning new weapons systems, where the costs are small in the research phase, grow far greater in the development phase, and still greater in the procurement and maintenance phases. Because the costs are comparatively very cheap in the first phase, it pays to start work on many more weapons than can possibly ever be fully developed and bought, and then to weed out those that prove less promising before they get into the billions of dollars phases. But this can only be done if there is a really firm will to weed out the less promising weapons as soon as it becomes apparent that they cannot compete with alternative developments that can do a given job more cheaply. This is not an easy thing to do. Once a development program is begun a lobby inevitably develops inside the Pentagon, among the industrial contractors working on the project, and in Congress, to keep the thing going. The pressure is always to keep going on whatever has been begun, which leads to the tendency not to begin things whose promise is unclear, and this in turn leads to excessive conservatism in starting research programs unless, of course, the top officials have confidence that they can kill projects almost as easily as they can start them.

### Advantages

The new budget system, as noted earlier, attempts to bring together clearly all the costs of a program, not only through development, but through procurement and operation, and brings these estimates into clear contrast with alternative developments. This will, it is hoped, not only give a clearer basis for making tough decisions, including decisions to kill programs, but by making the contrast explicit tend to force decisions which in the past it has been easier to shuffle out of sight.

The second difficulty, that there is no guarantee that Congress will appropriate the money needed in future years to make the first year's investment make sense, is far less of a problem than it sounds. As a practical matter Congress puts up the money. Everyone in Congress, for example, understands that the big increase in the space program for this year makes sense only on the assumption that money will be available to continue the accelerated program in future years, and that in voting the \$1.7 billion for this year Congress has in effect fully committed itself to putting up, year by year, the rest of the \$20 billion or more that will be needed for

the rest of the decade. Government officials are not always happy with this sort of assumed, but not formally assured, continuation of support. But they are familiar with what is going on and have learned to live with it. Where the theoretical uncertainty becomes important is when the government has to gain the confidence of people outside the government. With foreign aid, for example, it is hard to explain to foreign governments, not familiar with the peculiarities of the American political system, how the foreign government can with confidence undertake a long-term project dependent on American assistance, when the American negotiators have no legal authority to assure them that the money for future years will be available. In the sciences, a similar problem arises in, for example, the effort of the government to sponsor long-term programs in materials research in a number of universities. The university officials and the scientists who are asked to work on the projects tend, not too surprisingly, to be uneasy at the thought that their money could be cut off the year after next when they are in the middle of a long-range program. To meet this problem of providing assurance the device of "no-year" appropriations has been gradually spreading, under which Congress appropriates money with a clause permitting a department to keep the money until it is all spent. Without the special clause the money would revert to the Treasury at the end of the fiscal year, and a new appropriation would have to be gotten. Using no-year appropriations the Defense Department has set up 5-year funds for the materials research programs, which give the universities involved assurance of a minimum amount of support that will be available. Each year a new appropriation is gotten, so perpetuating the 5-year fund and the assurance of a minimum level of support for 5 years in the future.

The trend is for such devices to circumvent the year-by-year appropriation procedure to grow a bit commoner each year. But the process is more of erosion of the year-by-year Congressional control than of a formal effort to reform the whole budget process. There is a wide body of opinion that is convinced that a general reform of the budget procedure is overdue, but the Congressional appropriations committees are not anxious to give up the extra measure of power that comes with the ability to cut off a program in mid-stream. Although the power is hardly

ever used, the threat of its use, indeed the mere possibility of the threat of its use, gives the appropriations committees, and especially the chairmen of appropriations subcommittees handling the various departments, a little extra leverage in winning Administration support for projects they particularly support. On more general grounds, Congress is never anxious to relax whatever power it has over the executive branch, any more than the executive branch is ever anxious to restrict whatever freedom it has from Congressional control, and to this is added the feeling among a good many conservative members of Congress that the government is always spending too much money anyway, and the spending will only be higher if the budget process were made less awkward. The result is that the frequent proposals for a formal over-all reform of the budget process never seem to get anywhere, but in the face of necessity, now in one area, now in another, the erosion of the year-by-year control goes on.

#### Overlapping Programs

A different kind of budget problem comes up in dealing with programs that overlap several departments, and which are therefore difficult to fit into the neatly departmentalized budget. The oceanography program, for example, is scattered among nine major independent agencies and cabinet departments, and within them among 25 or so smaller agencies and offices. There is no single appropriations subcommittee to whom the program as a whole can be submitted. But neither the Eisenhower Administration nor the Kennedy Administration have taken kindly to suggestions that the whole program be put under the jurisdiction of the National Science Foundation, which would present the unified program to a single appropriations subcommittee in the Senate and in the House, and then distribute the funds among the various agencies that are taking part in the program. This opposition is partly on the grounds that the oceanography budget, now about \$100 million a year, is nearly 40 percent as large as the total NSF budget, and that the role of NSF would be unbalanced if it tried to digest this sum and devote so much of its energies to the single area of oceanography.

The executive branch has shown even less enthusiasm for the proposal of Senator Magnuson, to write into the law an authorization of a 10-year pro-

gram in oceanography. Magnuson's proposal also includes giving the central responsibility to NSF. The opposition to the 10-year part of Magnuson's proposal comes because it would write a specific program of research into the law—so much for ships, so much for training grants, and so on—and while everyone is for long-range planning, the Administration does not want to be tied down to a given course of action as rigidly as by writing the long-range plan into law. The Magnuson bill passed the Senate last week, as a similar bill did last year, but with the knowledge that, as last year, it will almost certainly die in the House. The passage of the bill was more of a reflection to Magnuson's prestige among his fellow Senators and his power as chairman of the Commerce committee and of the appropriations subcommittee that handles the space program and the NSF, than of a real determination in the Senate to write the 10-year program into law whether the Administration likes it or not.

The tendency of the executive branch, under Eisenhower, and so far under Kennedy, has been to avoid asking for major reforms, but to try to work out more or less informal arrangements to meet a given problem. In oceanography, this has involved such things as including references to the importance of oceanography in several of the President's major addresses and messages to Congress; the preparation of the booklet bringing together all the elements of the program and distributing it to the members of the appropriations subcommittees that must consider various parts of the program; and the organization of an interdepartmental committee on oceanography, chaired by the assistant secretary of the Navy for research and development (the Navy puts up the largest share of the programmed money), whose responsibility is to work out a recommendation to the President for an overall program and to see that the agencies involved include their share of the program in their budgets. The responsible officials seem satisfied that these modest steps are winning the desired support for the interagency program, and so long as such small steps seem adequate to do the job, they are not much tempted to get into the sticky jurisdictional haggling among the executive agencies and among the Congressional committees that would have to be faced if a general reform of the procedure were proposed.—H.M.



## News Notes

### Weather Research

President Kennedy recently cabled his deep sympathy to Japan for the disastrous rains that flooded parts of that country and caused more than 1500 casualties, and damages officially estimated at \$422 million. Typhoons as well as torrential rains have annually taken a heavy toll of lives and property in Japan as well as elsewhere in the Far East and Southeast Asia, mainly because scientific techniques for early detection and warning have not been developed sufficiently to permit adequate advance preparation and safeguards. Many of these destructive storms form near the equator in areas practically devoid of weather information; and frequently the first warning of such a storm is after it strikes an island, ship, or continental shore line. Presently Tiros III, America's latest weather satellite, placed in orbit 50 degrees north and south of the equator 30 days ago, is providing meteorological observations previously unavailable in these data-sparse regions by measuring earth-atmosphere energy exchanges through infrared sensors and by photographing cloud formations.

The rate at which various energies enter and leave the atmosphere may have a profound effect on weather, but the full possibilities of such data cannot be realized until techniques have been developed to fully utilize and evaluate them. However, observations have demonstrated that weather phenomena are accompanied by cloud patterns. Spiral cloud bands, for example, are associated with tropical cyclones; hurricane clouds have similar banding but are smaller and move faster than cyclone clouds, and certain storm-producing clouds cannot be detected by surface meteorological observations. Such cloud pictures were made available to Japanese meteorologists from Tiros III in its first 17 days of operation. They have proved so valuable that Kiyoo Wadachi, the chief of Japan's weather bureau, is hopeful that cloud data to be obtained from the satellite when it again orbits near Japan during 18 August to 25 September, a period expected to be high in typhoon activity, may open a new era in forecasting typhoons and storms.

At the same time, Tiros III also will be providing data that will improve national ability to forecast hurricanes thus demonstrating it is no burden to a satellite system to satisfy national requirements as well as those of the in-

ternational community. Previous Tiros pictures were made available to all nations that could benefit from them, including Russia. And, according to the U.S. Weather Bureau, any nation that desires can, "at minimum expense," establish local stations to obtain cloud pictures in its immediate vicinity.

Complementing the hurricane detecting capabilities of Tiros III, the U.S. Weather Bureau recently announced that Nomad I, the first in a series of seven ocean-floating electronic weather robots, will be anchored in the Gulf of Mexico about 300 miles south of New Orleans in the area where hurricanes develop. The robot station, a 10- by 20-foot platform equipped with weather gear, will gather information on air and water temperatures, barometric pressure, wind speed and direction, and the direction of ocean surface currents and will transmit in code made available to private or governmental agencies. Anyone with a short-wave receiver will be able to pick up the signals. The seagoing Nomad, like the airborne Tiros, can report data from areas that are not conveniently accessible by manned vehicles.

From Nomad, Tiros, other future weather satellites, and more conventional techniques, meteorologists hope to be able to understand the development of atmospheric movements so that slight modification in weather may be possible. The aim is to be able, for example, to break up storms before they reach the severe stage, or to redirect rain-producing clouds over drought-stricken areas. But meteorologists will conduct such experiments with extreme caution, since wrong weather modification methods could lead to worse weather rather than improved conditions.

### Missile Medicine

An instrument used in the guidance system of the Polaris missile has yielded new data about the viscous character of blood which may lead to greater understanding of circulatory disorders and cardiovascular disease. The new data disproves a previously accepted theory that blood is a Newtonian fluid, one whose thickness or viscosity remains unchanged no matter how fast or slow it is moved. (Water is a Newtonian fluid. Catsup or mayonnaise are non-Newtonian; rate of flow varies their thicknesses.)



Navy Hurricane Hunter flying above typical hurricane cloud formation. [Courtesy U.S. Navy]



## Announcements

A group of scientists—297 chemists and 404 physicists—recently were wired for sound in connection with a study of **scientists' professional reading habits**. Each participant was given a "random alarm mechanism," an electronic device the size of a package of cigarettes designed to emit audible alarms at random moments. If the scientist was reading a scientific periodical when the alarm sounded, he filled out a short questionnaire indicating the nature of his reading matter. Results of the 14-day study, sponsored by the National Science Foundation and conducted by Case Institute of Technology, show that U.S. physicists and chemists do not read more than an estimated 5 percent of the current professional literature published in their fields. (Office of Technical Services, Department of Commerce, Washington 25, D.C. Order No. PB 171 503. \$2)

The American Institute of **Chemical Engineers** is soliciting suggestions of research needs to become a part of a compilation to be made by its newly formed subcommittee on research needs. The subcommittee is to be a clearing house for research ideas in its field. (Frank C. Croxton, Battelle Memorial Institute, 505 King Ave., Columbus 1, Ohio)

Copies of the printed Congressional hearings on applications of **radioisotopes and radiation** in the life sciences and a summary-analysis of these hearings, which were held 27–30 March 1961, have been made available by the Joint Committee on Atomic Energy. (Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C.)

A **Conference on Science Manuscripts** has been organized to stimulate scientists and scientific organizations to take adequate steps to preserve records which will be useful source materials for future historians of science. The organization developed out of a meeting held in Washington last December, supported by the National Science Foundation, where a good deal of concern was expressed over the adequacy of current efforts in this direction. As a first project, the conference hopes to encourage the compilation and distribu-

tion to the scientific community of a guide summarizing the kind of material that should be preserved and ways in which this can be accomplished. The conference invites inquiries from interested individuals and organizations. (Nathan Reingold, Science and Technology Division, Library of Congress, Washington 25)

A special task force has been formed by the Public Health Service to make recommendations on a **program to eradicate syphilis** as a public health problem in the United States. The formation of the "emergency group" was prompted by the report of 19,000 cases of infectious syphilis in fiscal year 1961—the greatest number reported since 1950. Since 1956 there has been an increase of more than 130 percent in cases reported among individuals under 20.

The results of the study, organized at the request of the subcommittee handling PHS funds, will form the basis of a special report to the House Appropriations Committee at the next session of Congress.

"Highlights of **Research Progress in Allergy and Infectious Diseases, 1960**," a publication issued by the U.S. Public Health Service, reviews 50 research projects conducted by PHS's Institute of Allergy and Infectious Diseases or by other organizations to which the institute had made research grants. (Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C. \$0.30)

Applications are being accepted from colleges and universities that wish to use the Oak Ridge **mobile radioisotope laboratory** during the academic year 1961–62. The 35-foot laboratory-on-wheels, designed to travel to campuses of smaller colleges and universities, is used for conducting 2-week courses on radioisotope techniques. It is staffed by two Oak Ridge scientists, who act as course directors, and can accommodate six participants at each teaching session. (Mobile Laboratory Program, Oak Ridge Institute of Nuclear Studies, Post Office Box 117, Oak Ridge, Tenn.)

Summaries of the papers to be presented to the United Nations conference on **new sources of energy** (Rome, 21–31 August), the papers themselves, background information on the tech-

nical topics, or the full list of papers and the names and countries of participants are available to interested parties. (Central News Desk, Office of Public Information, Room 284, United Nations, New York) [*Science* 133, 318 (3 Feb. 1961)]

The AEC will no longer routinely produce and distribute **cobalt-60**, a radioactive isotope used in medical research. This is in accordance with AEC's general policy of discontinuing services and distribution of material when these become available from commercial sources. The isotope is now being produced in the test reactors at Westinghouse and at General Electric in quantities sufficient to meet ordinary demands. The AEC will continue to provide single shipments of cobalt-60 in excess of 100,000 curies, at a cost of \$1 per curie.

## Meeting Notes

The second international congress on **information processing** will be held in Munich from 27 August to 1 September 1962. (Information Processing Societies, 142 Great Road, Bedford, Mass.)

**Atom Fair-61**, the annual trade fair of the atomic industry, will be held from 6 to 9 November at the Conrad Hilton Hotel, Chicago, in conjunction with the annual meetings of the American Nuclear Society and the Atomic Industrial Forum. Special passes for business, scientific, industrial, and government personnel are available on request. (Atomic Industrial Forum, 850 3rd Ave., New York 22)

A government-industry symposium on **oceanographic instrumentation** will be held 16 and 17 August at the Department of the Interior, Washington, D.C. Because of limited space, advance registration will be required. (Donald L. McKernan, Interagency Committee on Oceanography, Department of the Interior, Washington 25)

A symposium on the **experimental method in biology** from the time of Antonio Vallisneri (1661–1730) to the present will be held at the University of Padua from 29 September to 1 October. Members of cultural institutions and students of the history of biology and the methodology and philosophy

of natural and medical sciences are invited to attend. (Organizing Committee, the University of Padua, Via 8 Febbraio, Padua, Italy)

The newly formed **American Society for Cell Biology** will hold its first meeting 2-4 November at the Edgewater Beach Hotel, Chicago. Deadline for 300-word abstracts: *15 August*. [Hewson Swift, Department of Zoology, University of Chicago, Chicago 37, Ill. (abstracts); M. J. Moses, Box 2982, Duke University School of Medicine, Durham, N.C. (information)]

A **biomagnetic symposium**, planned to bring together all individuals interested in this field, will be held 24-25 November at the University of Illinois. (M. F. Barnothy, University of Illinois, 833 S. Wood St., Chicago)

### Grants, Fellowships, and Awards

The National Science Foundation's **graduate laboratory development** program is offering grants to institutions of higher education to aid in modernizing, renovating, or expanding graduate-level basic research laboratories. Only those departments having a graduate training program leading to the doctoral degree in science at the time the proposal is submitted are eligible. Deadline: *1 September*. Proposals received after the deadline will be reviewed after 1 March 1962, the next closing date. (Office of Institutional Programs, NSF, Washington 25)

The **General Thomas D. White Space award** has been established by the National Geographic Society to "encourage and inspire further conquests of space." The award will be presented annually "to that military member or civil service employee of the Air Force who has made the most outstanding contribution to the Nation's progress in aerospace."

Fellowships in **marine planktonological research**, to be conducted at the Sandy Hook Marine Laboratory, are being offered by Columbia's Lamont Geological Observatory. The fellowships, open to qualified scientists of any nationality, will be limited, in general, to \$1500 plus transportation. A research vessel is available at Sandy Hook for field collecting. (Director, Sandy Hook Laboratory, P.O. Box 428, Highlands, N.J.)

### Scientists in the News

**Edward Wenk, Jr.**, has been named technical assistant to Jerome B. Wiesner (Special Assistant to the President for Science and Technology) and executive secretary of the Federal Council for Science and Technology. Wenk was formerly senior specialist in science and technology with the Legislative Reference Service of the Library of Congress.

**Richard Trumbull** has been appointed head of the Psychological Sciences Division, Office of Naval Research, succeeding **Denzel D. Smith**, who resigned to join the staff of the National Science Foundation. Trumbull was formerly head of the division's physiological psychology branch.

**James D. Hardy**, recently appointed professor of physiology in the Yale University School of Medicine, has been named director of the John B. Pierce Foundation's New Haven Laboratory.

**Graham Hoyle**, of the University of Glasgow, and **Seymour Shapiro**, of Brookhaven National Laboratories, have been appointed professor and associate professor of biology, respectively, at the University of Oregon.

**Victor F. Weisskopf** has been appointed the fourth director-general of the European Organization for Nuclear Research (CERN) in Geneva. Weisskopf, a former member of the organization's research directorate, succeeds **J. B. Adams**, who has been named director of the Controlled Thermonuclear Research Establishment, Culham, England.

**Paul E. Lacy**, assistant dean of the Washington University School of Medicine, has been named Mallinckrodt professor and head of the university's department of pathology.

**Dieter H. Sussdorf**, research fellow in immunochemistry at the California Institute of Technology, has been awarded the Royal Society of Edinburgh's David Anderson-Berry prize.

**John W. Knutson**, chief dental officer with the U.S. Public Health Service, has been appointed professor of preventive dentistry at the new University of California (Los Angeles) School of Dentistry.

**John A. D. Cooper**, professor of biochemistry and associate dean of Northwestern University Medical School, has been named dean of the University of Miami School of Medicine.

**John C. Hume**, chief of the health division of the U.S. Technical Cooperation Mission to India, has been appointed professor of public health administration at the Johns Hopkins School of Hygiene and Public Health.

**Klaus L. Cappel**, principal engineer in the Franklin Institute's Applied Mechanics Laboratory, has been named manager of the institute's new Aerospace Laboratory.

**Steven J. Taussig**, a chemical engineer in Rumania until his arrival in the United States last year, has been named technical director of Pacific Laboratories, Inc., Honolulu.

**Felix Morley**, chairman of the trustees of the Institute for Social Science Research, Washington, D.C., has won the \$15,000 1961 William Volker Distinguished Service award.

**Arthur H. Compton**, Nobel laureate, has retired as professor of natural philosophy at Washington University to accept an appointment as professor-at-large of the University of California.

### Recent Deaths

**J. R. B. Hutchinson**, 58; consultant in cardiology at Arlington Hospital, Va., and vice president of Acacia Mutual Life Insurance Co.; 1 Aug.

**Norman Jolliffe**, 60; director of the New York Department of Health's bureau of nutrition since its creation in 1949; 1 Aug.

**A. W. McCullough**, 60; professor of anatomy at the University of Arkansas Medical Center; 19 July.

**Norman E. Phillips**, 67; head of the department of zoology at the University of Maryland until his retirement in 1955; 1 Aug.

*Erratum:* The Xth International Congress of the History of Science will be held at Cornell University, Ithaca, New York, from 26 August to 31 August 1962 and at the American Philosophical Society in Philadelphia from 31 August to 2 September 1962. The closing date for the submission of abstracts is 1 May 1962. All correspondence should be directed to the Secretary, Xth International Congress of the History of Science, Cornell University, Ithaca, New York. This meeting has been erroneously listed in the Forthcoming Events section of recent issues.

## Book Reviews

### Peroxide, Axes, and Aspirin

**Mambu. A Melanesian millennium.**  
Kenelm Burridge. Humanities Press,  
New York, 1961. xxiii + 296 pp.  
Illus. \$8.50.

During the present century the native peoples of Melanesia have produced dozens of millenarian religious movements. These Melanesian movements are generally called "cargo cults" by Europeans. Comparable religious movements have been recorded among Indians of North and South America, among Negroes of Africa, and, indeed, among most of the tribal peoples of the earth. Historians and sociologists have studied similar events in the history of the major civilizations. Recently these movements, in both tribal and urban cultures, have attracted much attention from anthropologists, and there has been a small spate of theoretical and descriptive writing on the subject of what are variously termed nativistic movements, revitalization movements, cargo cults, and the like, particularly among tribal peoples in the throes of acculturation to Western civilization. In such movements there is usually a revolutionary code which defines the existing society as evil and which urges action—rational or irrational, magical or realistic, religious or political—to bring about a better state of affairs.

In the early 1950's Burridge spent some time with the people of Tangu, a small tribal group in the Australian Trust Territory of New Guinea. Although he did not observe a cargo cult in full flower, Burridge was able to learn much of the oral history of two such recent cults, and he was further able to study the climate of experience, belief, and emotion in which such cults develop. The title of this book, *Mambu*, is the name of one of the earlier prophets who led an abortive cargo movement.

Although the people involved in the narrative are few and their customs and beliefs exotic, or even bizarre, to Western eyes, the larger point which Burridge makes is obligatory for an understanding of the motive which brings many tribal (and civilized) peoples to participate in such movements generally. This motive is the desperate wish to establish an identity as competent and respectable human beings in some sort of morally equivalent relationship with a dominant alien people. The bulk of the book is devoted to analyzing the combinations of native culture, historical circumstance, and moral pressure exerted by missionaries and Australian administrators which have caused the Tangu to see the portal to manhood as a religious movement which anticipates a millennium. This millennium, with its cargo of hydrogen peroxide, axes, aspirin, rice, and so forth, is but the symbol of the achievement of equality with, and acceptance by, the "moral European."

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### Chromatography Handbook

**Handbuch der Papierchromatographie.**  
vol. 1, *Grundlagen und Technik*.  
1958. 860 pp. Illus. \$14.60. vol. 2,  
*Bibliographie und Anwendungen*.  
1960. 726 pp. \$11. I. M. Hais and  
K. Macek, Eds. Gustav Fischer,  
Jena, East Germany.

The forerunner of these volumes, *Papirova Chromatografie* (I. M. Hais and K. Macek Eds., Czechoslovakian Academy of Sciences, Prague, 1954), was reviewed in *Science* 6 years ago [122, 473 (1955)]; but the volumes are not a translation into German of the earlier Czechoslovakian volume, nor

are all of the collaborators the same. Volume 1 contains the work of 22 collaborators, including the editors.

As far as I can tell, they comprise the most authoritative monographs on paper chromatography available. Their distinction rests not only on the breadth of the literature coverage, which extends to the end of 1956, but also, and chiefly, on the approach. This combines, in volume 1, practical instructions with theoretical enquiry into the principles which can be derived from practice and which should guide new work. In other words, the subject of paper chromatography is treated as a science, as in the previous volume, but now with more years of experience and published work to draw upon.

Volume 1 provides a brief historical chapter in which are reproduced in color two plates from Runge's early work and six examples of capillary analysis. This chapter includes photographs of Consden, Gordon, Martin, and Synge. The second chapter deals with principles and theory in a clear and lavishly illustrated manner. Then follow five chapters in which every step of the process is described in detail, with discussion of the influence of various factors such as the nature of the paper, the effect of shape and position of initial spot (or zone), and so on. Included also are sections on outfitting a laboratory, working with radioactive substances, and carrying out paper chromatography on a preparative scale. These chapters complete the general part of the book: some 224 pages, including a bibliography for each chapter.

The special part of the book contains chapters into which separations are gathered in terms of functional group and molecular class: alcohols, carbonyl compounds, aliphatic acids, carbohydrates, phenols and aromatic acids, steroids, hydrocarbons and other lipophilic substances, amines, nitro-compounds, amino acids, peptides, proteins, purines and pyrimidines, alkaloids, other heterocyclic nitrogen compounds, organic sulfur compounds, vitamins, antibiotics, insecticides, synthetic pigments, and inorganic substances. Each chapter has its own bibliography.

The final part of the book continues an important feature of the earlier volume, namely a section on reagents (189 in number) for detecting spots, with recipes, and in many cases alternative recipes. This is followed by a section of some 144 items bearing on



the preparation and impregnation of paper, the choice of solvent systems, converting substances to forms more suitable for chromatography (such as converting acids to hydroxamic acids), preparing samples for chromatography, and carrying out quantitative analyses. These two sections are detailed and represent a valuable compilation of frequently needed data. Finally, there are author and subject indexes (39½ pages, each with two columns of entries).

Volume 2, an important adjunct to volume 1, contains a minimum of explanatory text and 10,290 bibliographic entries, each with author, title or indication of the subject dealt with, and reference. These are also organized into two main divisions: a general part (56 pages) and the special part which comprises the bulk of the volume. The special part is divided into chapters which deal with particular types of compounds, some of which have been added since volume 1 was published. Most of the chapters are further subdivided. For example, the chapter on organic acids is subdivided into general reviews, lower fatty acids, higher fatty acids, aliphatic hydroxy acids, di- and tricarboxylic acids, keto acids, phenolic and other cyclic acids, glycerides and other esters of organic acids. Most of these subdivisions are further classified in terms of techniques and applications, which are themselves further subdivided. This careful, logical organization makes the information extraordinarily accessible down to very narrow requirements. The volume concludes with a complete author index and an alphabetical index of substances that have been chromatographed. The references in volume 2 comprise four times as many substances as are referred to in volume 1.

Both volumes are printed on good paper in a clear and readable style. The illustrations in volume 1 are excellently chosen, and the authors do not avoid epistemological considerations where these are appropriate—that is, where such considerations help the reader to understand the reasoning behind the method. For all of these reasons the editors and authors are to be congratulated on providing paper chromatographers, from beginners to experts, with a first-rate text and reference work. I recommend the two volumes most highly.

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## Quantitative Science

**Experimental Immunochemistry.** Elvin A. Kabat. With chapters by Manfred M. Mayer. Thomas, Springfield, Ill., ed. 2, 1961. xii + 905 pp. Illus. \$26.50.

For those familiar with the 1948 edition of Kabat and Mayer, the publication of Kabat's new edition is an important event. Michael Heidelberger in the preface (an introduction) to the first edition predicted that *Experimental Immunochemistry* would be "more likely to gather acid spots and indicator stains on the laboratory table than to accumulate dust on the reference shelf," and I am prepared to produce the shreds of my second copy as the fulfillment of Heidelberger's prophecy.

Immunochemists and their forebears, immunologists, recognize that immunochemistry became a discipline in its own right through the brilliant and precise efforts of small groups of chemists and biologists to render quantitative an otherwise empirical science. The discipline, however, has evolved during the past decade into a bureaucracy, which even an author possessed of the breadth and clarity of Kabat finds impossible to treat fully in more than twice the lineage of the first edition (900 two-column pages versus 550 single-column pages). Consequently, the author felt justified in omitting discussions of some newer offshoots of immunology, such as immunohistology and immunohematology, possibly because they do not as yet lend themselves to analysis by many of the precise quantitative methods with which the book is primarily concerned.

The original format has been preserved. There are four parts dealing with basic methodology and theory, applications, chemical and physical methods, and preparations. Several new chapters have been added to provide introductions to interim developments such as chromatography and measurements of radioactivity. Many chapters are greatly enlarged. The section on complement and complement fixation, by Mayer, is nearly three times more copious; it has new illustrations and tables. An excellent treatment of electrophoretic methods now includes discussions on the applications and limitations of various zone-electrophoresis techniques, including immunoelectrophoresis.

Gel-diffusion methods are now recognized among the most powerful tools available for analysis of complex antigen-antibody systems. They are treated

extensively, but more from the theoretical than technical aspect. For the purposes of this book such a presentation is proper since the power and wide application of most techniques derive as much from their versatility as from their inherent physical or chemical qualifications. Because they are versatile, gel-diffusion methods have been modified in many ways by individual investigators to suit their particular problems.

The author's discretion in such matters demonstrates considerable insight into the basic questions which investigators pose for reference handbooks—for example: How can our results best be interpreted? Wherever appropriate, Kabat has provided theoretical and practical guideposts and danger signals in the application of physical and chemical methods to immunochemistry and in the use of immunochemical tools in approaches to biological or biochemical problems. In this respect *Experimental Immunochemistry* is not only an immunochemist's volume. It is a major contribution toward the advancement of the biochemistry of macromolecules, and it is to be highly recommended to all chemists and biologists whose fields are beginning to feel the impact of practical and theoretical immunochemistry.

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## Chloroplast

**The Life of the Green Plant.** Arthur W. Galston. Prentice-Hall, Englewood Cliffs, N.J., 1961. 116 pp. Illus. \$2.95.

This concise, up-to-date summary of the fundamentals of plant physiology is chiefly designed for use in introductory courses in biology, but it should also be an ideal complement to more comprehensive texts used for beginning courses in plant physiology.

The sequence of topics is essentially the same as that in the larger text, *Principles of Plant Physiology*, by Galston and James Bonner. The most noticeable changes in content are the omission of the details of intermediary metabolism (which is to be expected, considering the audience for which this "Foundations of Modern Biology Series" is designed), the addition of a chapter on the green plant cell, and the emphasis on plant growth, differentiation,



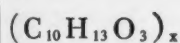
and morphogenesis (comprising almost half the book). As those who have used the *Principles* will expect, the work is lucidly written and well organized. Illustrations are of high quality and in good taste.

I have only minor criticisms: for example, on page 37 it is not at all clear why it follows from the action spectrum of photosynthesis that carotenoids must be involved in the process, and on page 79 possibly too much emphasis is placed on the survival value of bud dormancy. In such a condensation very few of those persons associated with the major advances in a field can be mentioned; in this case it would have been wise to omit names entirely.

I suspect many students will consider careers in experimental botany as a result of using this volume.

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**The Chemistry of Lignin.** Supplement volume. Covering the literature for the years 1949–1958. Fredrich Emil Brauns and Dorothy Alexandra Brauns. Academic Press, New York, 1960. x + 804 pp. Illus. \$18.

Some idea of the effort expended on lignin research during the decade covered can be gained by noting that the size of this volume is almost identical to that of the first, which dealt with the entire earlier period beginning with the discovery of lignin in the 1830's. Workers in the lignin field who have long since abandoned attempts to keep abreast of the flood of pertinent literature will find the appearance of this supplement most welcome.

Although readers expecting to encounter progress in proportion to the volume of research may well be disillusioned, some will consider excessively pessimistic the authors' view that little progress has been made toward the elucidation of the structure of lignin. Recent evidence, much of which is admittedly indirect, has at least permitted presentation of a plausible diagram representing the main types of lignin "building stones" and the linkages between them. Such a concept seems to be gaining increasing acceptance, and this is a welcome change from the multitude of often-conflicting theories extant in 1952.

In other areas of lignin research, notably the problem of the lignin-carbohydrate bond (discussed here by J. W. T. Merewether) and the lignification process, very significant advances are reported. In recognition of this, for example, the chapter formerly entitled "Theories on the formation of lignin" now appears as "The biosynthesis of lignin."

Otherwise the plans of the volumes are virtually identical, although there have been considerable shifts of emphasis. The entire spectrum of lignin research has been scanned with such thoroughness and attention to detail that for many purposes reference to the original literature will be unnecessary. Especially gratifying in this respect are the frequent reproductions of tables, figures, and experimental procedures from Japanese, Soviet, and other journals not always readily accessible to American readers. As before, Brauns writes critically, exhibiting a profound knowledge of his subject, and he maintains a disinterested viewpoint even in areas where vigorous controversy has sometimes been in evidence.

The present volume, with its predecessor, can be regarded justifiably as the standard treatise on lignin in the English language, and it merits a place in the library of anyone seriously interested in the field.

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## Fatal Genes

**Developmental Genetics and Lethal Factors.** Ernst Hadorn. Translated by Ursula Mittwoch. Methuen, London; Wiley, New York, 1961. xviii + 355 pp. Illus. \$8.50.

Biologists can only be grateful for an English version of this most valuable monograph on lethal factors, although one may wish that the time interval between the appearance of the original German edition (1955) and the appearance of the English translation (1961) had been shorter.

Lethals are defined as "Mendelian units which cause the death of an organism prior to the reproductive stage." They arise by mutation, probably in all organisms from virus to man. Since Ernst Hadorn has contributed perhaps more than any other person to

their study, a painstaking and critical review from his pen of the now very extensive pertinent literature (the bibliography alone covers 32 pages) is very useful. Investigations made with lethals in *Drosophila*, mouse, and poultry are considered most fully, but other organisms, including plants and microorganisms, are by no means overlooked. Nor are human lethals neglected, although, of necessity, the coverage is here least comprehensive. A book as large as the present one would be needed to deal with lethal and semilethal hereditary diseases and malformations in man alone.

The bearing of the studies of lethal factors on the problems of developmental genetics is, as indicated by the title of the book, in the center of the author's attention. Brief descriptions of the occurrence of lethals in natural populations, of their economic importance, and of the possibilities of therapy's causing the otherwise lethal genotypes to produce viable individuals are nevertheless included. All in all, this is an indispensable book in any biological library.

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## Using Groups in Physics

**The Application of Group Theory in Physics.** G. Ya. Lyubarskii. Translated from the Russian by Stevan Dedijer. Pergamon, New York, 1960. ix + 380 pp. \$10.

This English translation of a Russian work by G. Ya. Lyubarskii is a readable and quite complete discussion of the major applications that group theory finds in theoretical physics. The applications are discussed in sufficient detail to supply an interested reader with a working knowledge of the subject matter.

The book is very much slanted toward applications, and the early chapters, which discuss the general properties of groups and their representations, are quite sketchy. Complete descriptions of the properties and representations of groups of physical interest appear in the later chapters. Included in these discussions are the point groups, permutation groups, and space groups. Two entire chapters are devoted to the rotation groups in two and three dimensions, and another to the properties and

representations of the Lorentz group. Character tables are supplied for the permutation group (up to  $S_7$ ) as well as for the point groups. Included, as well, are abbreviated descriptions of all of the 230 crystallographic space groups.

When it comes to the applications of these groups to specific physical problems, the book seems at its very best. There are chapters discussing the application to normal modes of vibration, to electron energy levels in crystals, to equations invariant under the Euclidean group of motions and those invariant under the Lorentz group, to second order phase transitions, and to nuclear reactions, among others.

The book is suitable for a graduate-level course, and to this end, problems are provided to illustrate the subject matter. This course would have to follow a course in quantum mechanics, since the author assumes a knowledge of quantum mechanics throughout.

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## New Books

### Biological and Medical Sciences

**Advances in Morphogenesis.** vol. 1. M. Abercrombie and Jean Brachett, Eds. Academic Press, New York, 1961. 458 pp. Illus. \$12.50.

**Advances in Thyroid Research.** Transactions of the Fourth International Goitre Conference. Rosalind Pitt-Rivers, Ed. Pergamon, New York, 1961. 550 pp. Illus. \$20.

**Annual Review of Plant Physiology.** vol. 12. Leonard Machlis and Winslow R. Briggs, Eds. Annual Reviews, Palo Alto, Calif., 1961. 509 pp. Illus. + plates. \$7.

**Antibiotica et Chemotherapia.** vol. 9. O. Gsell and R. L. Mayer, Eds. Karger, New York, 1961. 188 pp. Illus. \$11.

**Asphalts and Allied Substances.** Their occurrence, modes of production, uses in the arts, and methods of testing. vol. 2, *Industrial Raw Materials.* Herbert Abraham. Van Nostrand, Princeton, N.J., ed. 6, 1961. 351 pp. Illus. \$10.75.

**Atlas of Human Anatomy.** Franz Frohse, Max Brodel, and Leon Schlossberg. Barnes and Noble, New York, ed. 6, 1961. 190 pp. Illus. \$2.95.

**Basic Physiology.** Fred E. D'Amour. Univ. of Chicago Press, Chicago, Ill., 1961. 664 pp. Illus. \$7.95.

**A Biology of Crustacea.** James Green. Quadrangle Books, Chicago, 1961. 195 pp. Illus. \$5.75.

**Bird Study.** Andrew J. Berger. Wiley, New York, 1961. 400 pp. Illus. \$9.

**Cell Heredity.** Ruth Sager and Francis J. Ryan. Wiley, New York, 1961. 422 pp. Illus. \$7.50.

**Cell Mechanisms in Hormone Production and Action.** Memoir of the Society for Endocrinology, No. 11. P. C. Williams and C. R. Austin. Cambridge Univ. Press, New York, 1961. 183 pp. Illus. + plates. \$7.50. Proceedings of a symposium held 3-4 May 1960.

**Comparative Physiology of Carbohydrate Metabolism in Heterothermic Animals.** Arthur W. Martin, Ed. Univ. of Washington Press, Seattle, 1961. 151 pp. Illus. + plates. Paper, \$3.50; cloth, \$4.50.

**Dynamics of Even-Aged Forest Stands.** M. S. Czarnowski. Louisiana State Univ. Press, Baton Rouge, 1961. 145 pp. Illus. \$5.

### Mathematics, Physical Sciences, and Engineering

**Atomic Energy Waste.** Its nature, use, and disposal. E. Glueckauf, Ed. Interscience, New York; Butterworths, London, 1961. 431 pp. Illus. \$14.

**The Book on Games of Chance (Liber de Ludo Aleae).** Gerolamo Cardano. Translated by Sydney H. Gould. Holt, Rinehart, and Winston, New York, 1961. 62 pp. Illus. \$1.50. Reprinted from *Cardano: The Gambling Scholar* (Princeton Univ. Press, 1953).

**Dynamic Analysis of Machines.** Joseph E. Shigley. McGraw-Hill, New York, 1961. 314 pp. Illus. \$7.50. Companion volume to Shigley's *Analysis of Mechanisms*, 1959.

**Evaluation in Mathematics.** Twenty-sixth yearbook. National Council of Teachers of Mathematics, Washington, D.C., 1961. 222 pp. Illus. \$3.

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# Reports

## Fatigue in Phasic and Tonic Fibers of Frog Muscle

**Abstract.** Single isolated phasic muscle fibers and small bundles of tonic fibers were directly stimulated in one-per-second twitch series by massive electrode shocks. During the stimulation period the isometric tension developed by the phasic fiber continuously decreased, first rapidly and then slowly. The tonic fibers behaved similarly, but showed much less fatigue than the phasic ones. In general, recovery of the fibers after cessation of stimulation also occurred in two phases.

It is known that striated muscle, when stimulated directly at frequent intervals, will fatigue (1). It has also been shown that single muscle fibers under direct stimulation will show a gradual decline of tension similar to fatigue of whole muscle (2). However, there is some controversy regarding this latter finding; Ramsey (3) states that gradual falling off of tension with continual stimulation of a single isolated fiber is due to injury, and that uninjured fibers will not show this gradual decline of tension with continual stimulation. Consequently, our work was undertaken to determine precisely the mechanical changes which take place in single phasic muscle fibers stimulated at frequent intervals, and also to compare the changes with those of similarly treated tonic muscle fibers. Since the underlying cause of fatigue is still unknown, these and future experiments will attempt to shed some light on this phenomenon.

Both single phasic fibers and small bundles (10 fibers or less) of tonic fibers were isolated from the semitendinosus

muscle of *Rana pipiens*. The fibers were mounted horizontally by their tendons in a Lucite dish containing 60 ml of phosphate-buffered Ringer's solution with 0.2 percent *d*-tubocurarine. During an experiment oxygen was bubbled through this solution, and this served not only to oxygenate the tissue, but also to stir the medium constantly. All experiments were performed at 10°C. The developed isometric tensions were measured with a special low-drift myograph consisting of a combination of two RCA 5734 transducer tubes (4), and were recorded photographically from an oscilloscope. The fibers were mounted between two parallel platinum-plate electrodes so that the entire length of each fiber could be stimulated instantaneously. For these experiments, the fibers were maintained at rest length and stimulated once per second with slightly super-threshold square-wave shocks of 0.3 msec duration.

In all cases reported here the isolated fibers after 60 min of equilibration following dissection could be stretched and could develop tetanic tensions reversibly, and were thus considered uninjured. The phasic fibers had a diameter of 72 to 93  $\mu$  and developed isometric tensions of 0.9 to 1.2 kg/cm<sup>2</sup> (thus about 50 mg per fiber) before fatigue. The tonic fibers, being much thinner (about 25  $\mu$  in diameter), could not be individually isolated, and so we used small bundles which developed tensions of 50 to 125 mg. For this report, no attempt was made to determine the intrinsic tension output of the individual tonic fiber.

It was found for single phasic fibers that as twitches were evoked at the rate of one per second the developed tension continuously decreased in two phases. As shown for a typical experiment in Fig. 1, there was first a relatively rapid drop of 60 percent within 4 min, followed by a much slower decay which continued until there was no response. No staircase variations were observed, and the initial tension of the fiber remained constant throughout the stimulation. The recovery of the twitch out-

put after the stimulus was removed occurred in two phases, a rapid restoration of 30 percent in 15 sec, followed by a slow recovery which approached the initial amplitude within 60 min.

The rise time of the twitch for phasic fibers, measured from the onset of tension to peak, increased during the fatigue process. For the experiment represented in Fig. 1, the rise time gradually doubled during the first 8 min of stimulation, going from about 55 to 110 msec, and then remained fairly constant. However, the relaxation time of the fibers, measured from peak to one-half of the developed tension, showed a very rapid and large increase in duration. As shown in Fig. 1, the relaxation time was doubled after 3 min of stimulation and continued to rise to four times the initial value after 9 min. As with the amplitude changes, the recovery of the relaxation time occurred in two phases, a rapid one followed by a slow recovery to the initial time. The recovery of the rise time did not show any rapid phase, but slowly approached the initial time.

The tonic muscle fibers presented a rather different behavior. During stimulation at the rate of one per second, the decrease in the twitch amplitude, though developing in two somewhat distinct phases, was at all times very much smaller than that of the phasic fibers.

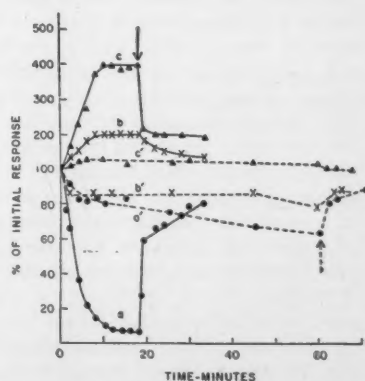


Fig. 1. Typical fatigue and recovery effects associated with a one-per-second twitch activity series of a single phasic fiber of 93- $\mu$  diameter (solid lines) and of a bundle of tonic fibers (dashed lines). Curves *a* and *a'* indicate changes of twitch amplitude; *b* and *b'*, rise time of twitch; and *c* and *c'*, relaxation time. The percentage changes are plotted relative to the response of the preparation just prior to the start of stimulation. The arrows mark the termination of activity and the beginning of recovery. (In cases where the fatigue of phasic fibers was followed in time beyond that shown here, the twitch gradually declined to zero.)

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should not repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to one 2-column figure (that is, a figure whose width equals two columns of text) or to one 2-column table or to two 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to contributors" [Science 125, 16 (1957)].



In a typical experiment as given in Fig. 1, after 4 min the twitch amplitude had dropped about 15 percent, and after 60 min it had declined only about 35 percent. After cessation of stimulation, the response increased 15 percent in 2 min and approached the initial amplitude at a slower rate. Both the rise and relaxation time remained fairly constant during the stimulation period, except for a change during the first few minutes; for the case shown in Fig. 1, the rise time decreased 15 percent during the first 2 min of stimulation, while the relaxation time increased 25 percent during the first 6 min of stimulation.

After each experiment, a potassium contracture (with 0.1M KCl) was recorded to check whether the fibers were phasic or tonic. Phasic fibers gave the usual contractures which relaxed after a minute or so, whereas the contracture of tonic fibers declined slowly over a period of many minutes.

Our finding that tonic fibers fatigue much more slowly than phasic ones confirms on the single muscle-cell level the previously made conclusion for such units derived from studies of the relative fatigability of corresponding whole muscles (5). Further research is required to determine whether there is any relation between this difference in fatigability and other fundamental properties distinguishing phasic and tonic fibers (6). The decrease in twitch output of a phasic muscle fiber occurs along a smooth curve until it finally fails completely to respond. Thus these fatigue changes and the corresponding ones we have observed in the tonic fibers are quite unlike the sudden total obliteration of response which Ramsey (3) describes, and which we also have seen, in a single fiber undergoing a tetanus of rather high frequency. Considering that the fatigue and recovery processes of the fibers occur, in general, in two steps, it would seem that fatigue may be attributed to two separate factors. The first may be due to changes in the excitation mechanism or in the excitation-contraction coupling, the second to changes at the level of the contractile mechanism. In elaboration of the results reported here, our future studies will deal with the effects of activity on the membrane process and with the role of individual fiber behavior in the development of fatigue of the whole muscle (7).

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29 March 1961

## Isolation of Abscisin, an Abscission Accelerating Substance

**Abstract.** A crystalline substance, designated *abscisin*, which accelerates abscission of excised debladed petioles at  $10^{-4}$  microgram per abscission zone, has been isolated from cotton burs. The yield was approximately 1 milligram from 10 kilograms of dry plant material.

The presence in plants of a substance (or substances) which accelerates abscission has been reported by several investigators. Osborne (1) found that the diffusates from senescent petioles of several plants accelerated abscission. Biggs and Leopold (2) discovered a factor from senescent leaves and fruits which accelerated abscission of debladed petioles. Herrero and Hall (3) found that extracts of pulvinoids from abscising leaves of cotton accelerate leaf abscission. Carns (4) and Carns *et al.* (5) reported that extracts of young cotton fruit walls accelerated abscission of debladed leaves and of young fruits. These findings, together with other evidence, led Addicott (6) to suggest that the substance(s) represents a new type of plant hormone, one that accelerates abscission. This report announces the isolation and preliminary characterization of such a substance

from cotton burs (dried, mature fruit walls after dehiscence and removal of seed and fiber).

The bioassay used to evaluate abscission-accelerating activity during the investigation was a modification of the explant test employed by Addicott *et al.* (7). Explants were cut from cotton seedlings when they were 18 to 20 days old. They consisted of 5-mm stumps of the cotyledonary petioles, 5 mm of the stem, and 10 mm of the hypocotyl. Test substances were applied in 1-percent agar as 0.005-ml droplets. Explants were held upright in stainless steel holders in petri dishes containing a layer of about 5 mm of 1.5-percent agar. Abscission was determined by the application of a uniform load of 10 g to the petiole stumps.

Approximately 134,000 ground cotton burs (364 kg) were extracted for 6 hr in batches with a total of 1725 liters of Skelly-solve B (petroleum ether, boiling point 60° to 75°C). The extract was concentrated to 9 liters in a falling-film concentrator. A 3-liter aliquot of this concentrate was extracted twice with 4.5 liters of a water-methanol (1:4) solvent, and the top lipid-rich layer was discarded. The methanol extract was taken to dryness and then exhaustively extracted with 5-percent sodium bicarbonate and filtered off, and the filtrate evaporated to dryness under reduced pressure. Subsequent extraction of the dried residue with anhydrous acetone yielded 10 g of an acetone-soluble solid which accelerated abscission in the explant bioassay at 5  $\mu$ g per abscission zone.

A sample of 5.7 g of the active solid was subjected to partition chromatography on a silicic acid column (6  $\times$  25 cm) that had been treated with sodium bicarbonate; water was used as the stationary phase (7 g of water per 10 g of adsorbent), and chloroform followed by *n*-butyl alcohol was used as the mobile phase (8). The butanol

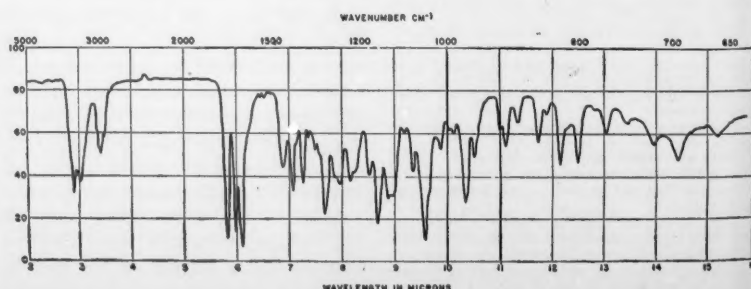


Fig. 1. Infrared spectrum of abscisin.



fraction contained 1.5 g of solid which accounted for most of the abscission-accelerating activity in the sample. A quantity of 0.8 g of this material was rechromatographed on a similar column (3.5 × 20 cm), chloroform being used as the eluting solvent. A number of visible bands separated on the column, characterized in the order of dark-brown, yellow, yellow, yellow, and red. The third band was found to be highly active, and from it abscisin was induced to crystallize as diagonal prisms from ethyl acetate. The crystalline substance accelerated abscission in the cotton explant test at a quantity as low as 10<sup>-2</sup> μg per abscission zone. In a typical experiment, for example, when abscission was determined 64 hr after the application of abscisin, the controls had 40 percent abscised while the explants with abscisin at 10<sup>-2</sup>, 10<sup>-1</sup>, and 1 μg per abscission zone had 52, 60, and 82 percent abscised, respectively.

The compound was crystallized to a constant melting point of 197° to 198°C, with a yield of 3 mg. Abscisin is an acidic compound soluble in chloroform and dilute sodium hydroxide, slightly soluble in ether but insoluble in dilute hydrochloric acid. It contains 67.93 percent of carbon and 6.26 percent of hydrogen. Its ultraviolet absorption maximum in methanol is at 250 mμ, and its infrared spectrum in KBr pellets is shown in Fig. 1 (9).

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9. This investigation was supported in part by funds from the National Cotton Council administered through the U.S. Department of Agriculture. The assistance rendered by the U.S.D.A. Fruit and Vegetable Laboratories, Pasadena, Calif., in making their facilities available for the extraction and concentration of the plant material, is gratefully acknowledged. We are particularly grateful to Dr. F. T. Addicott, Department of Botany, and Dr. Charles A. West, Department of Chemistry,

University of California, Los Angeles, for their interest and advice, and to Mrs. J. L. Lyon for her technical assistance throughout the investigation.

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2 April 1961

### Effect of Major Meteoric Showers on the Densities of the Upper Atmosphere

According to the recent results obtained by satellite measurements, reported by Lagow and Alexander (1), Dubin (2), and Nazarova (3), the amount of meteoric dust entering the earth's atmosphere is quite significant. From their data we have found that during a major meteor shower the energy injected by these particles into the atmosphere is sufficient to raise the temperature at 110 km by at least 5°K. This rise in temperature should produce an increase in density at the higher levels by 5 to 10 percent. A preliminary analysis of the density data obtained by drag measurements on the satellites at 300 and 600 km indicated a small rise in density on the day of a major meteoric shower.

Our calculations are based on data which indicate that the daily accretion rate of the interplanetary dust is of the order of 10<sup>6</sup> g. This implies a rate of approximately 2.10<sup>-12</sup> g cm<sup>-2</sup> sec<sup>-1</sup>. If the mean velocity of these particles is assumed to be 30 km/sec, the energy brought in is found to be approximately 1.10<sup>-3</sup> erg cm<sup>-2</sup> sec<sup>-1</sup>.

During a major meteoric "shower" the rate of influx of particles increases by a factor of 10 to 100, although Nazarova (3) reported an increase by a factor of 10<sup>4</sup> on 15 May 1958, which was attributed to a major meteoric stream (probably O-cetids). If, however, an increase by only a factor of 20 in the particle density during an average "major shower" is assumed, the energy input into the atmosphere will be as high as 0.2 erg cm<sup>-2</sup> sec<sup>-1</sup>. (A conservative value of velocity has been used. Major showers are known to have velocities up to 65 to 70 km/sec, which implies an increase in energy by another factor of 4.)

The energy brought in by the meteor particles can be given up to the earth's atmosphere, probably in the 100 to 120 km region, in three possible ways: (i) luminous radiation, (ii) ionization, and (iii) heating.

According to Whipple, the "luminous efficiency" factor for the meteoric particles is given by

$$\tau = \tau_0 V$$

where log  $\tau_0$  is -9.07 and  $V$  is the velocity of the particle (3 × 10<sup>6</sup> cm/sec), giving

$$\tau \approx 3 \times 10^{-3}$$

that is, only 0.3 percent of the energy will go as visible radiation. This can be regarded as negligible.

The "ionization efficiency factor," as given by Kaiser, is 0.1. The remaining 90 percent of the energy—that is, 0.18 erg cm<sup>-2</sup> sec<sup>-1</sup>—therefore goes immediately in heating. Since the major meteoric showers last, on an average, at least several hours, the energy available for heating the E-layer is of the order of 600 erg cm<sup>-2</sup> hr<sup>-1</sup>.

Table 1 gives the amounts of energy per square centimeter column required to heat the atmosphere above the altitude  $Z$  by 1°K, as calculated from the Jastrow-Kyle atmospheric model (4).

As the table shows, if the meteoric showers give up their energy in the 110- to 120-km layer, this region will be heated up by 5°K in 6 hr. This increase in temperature will produce an increase in density in the upper layers of the atmosphere given by the following relation:

$$\rho(Z) = \rho(Z_0) \frac{T_0}{T_m} e^{-\int (mg/KT_m) dz}$$

where  $T_m$  is the molecular scale temperature and  $KT/mg = H$  (scale height).

Table 2 presents estimates of per-

Table 1. Energy required to heat the atmosphere above altitude  $Z$  by 1°K.

$Z$ (km)	Mass of atmosphere above $Z$ km (g)	Energy (erg/cm <sup>2</sup> column)
90	1.858 × 10 <sup>-3</sup>	2.207 × 10 <sup>4</sup>
100	3.366 × 10 <sup>-4</sup>	3.999 × 10 <sup>4</sup>
110	8.348 × 10 <sup>-5</sup>	9.917 × 10 <sup>4</sup>
120	2.796 × 10 <sup>-5</sup>	3.322 × 10 <sup>5</sup>
150	5.856 × 10 <sup>-6</sup>	6.957 × 10 <sup>5</sup>
200	1.756 × 10 <sup>-6</sup>	2.086 × 10 <sup>6</sup>

Table 2. Estimates of percentage density increases resulting from a 5°K temperature rise over a 10-km layer.

Layer	Increase (%) in density at altitude			
	120 km	200 km	300 km	600 km
90 to 100 km	6	8	9	10.5
100 to 110 km	2	5	6	7
110 to 120 km		3	3	4

centage density increases resulting from a 5°K temperature rise over a 10-km layer. The computations have been made by Kyle by adding 0.5°K/km to the temperature gradients of the Jastrow-Kyle model atmosphere in the three representative layers, 90 to 100 km, 100 to 110 km, and 110 to 120 km.

A first analysis of the density data inferred from the satellite measurements is consistent with the expected 5 to 8 percent density increases at 355 and 660 km during the major meteor showers. However, more accurate data on orbital decelerations will be required to confirm this hypothesis.

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- \* On leave from Physique de l'Atmosphere, Faculté des Sciences de Paris. National Academy of Sciences-National Research Council research associate with the National Aeronautics and Space Administration.

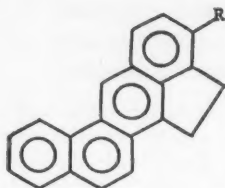
23 June 1961

### Polynuclear Aromatic Hydrocarbons, Steroids and Carcinogenesis

**Abstract.** In addition to the electronic factors, there is a steric factor responsible for the carcinogenicity of polynuclear aromatic hydrocarbons. A carcinogenic polynuclear aromatic hydrocarbon must bear steric resemblance to steroids. One possible implication to this requirement for carcinogenicity is that these hydrocarbons may act on the same sites as steroid hormones.

Numerous attempts have been made to correlate the carcinogenicity of polynuclear aromatic hydrocarbons and their structures by molecular orbital calculations (1), fluorescence spectra (2), absorption spectra (3), chemical reactivities (4), and abilities in molecular complex formation (5). All these approaches were based primarily on the electronic structure of the polynuclear aromatic hydrocarbons, and generally the carcinogenic hydrocarbons must possess low electronic excitation barriers. However, the overall results of these correlations are not satisfactory to account for the relative carcinogenicity of various alkylated polynuclear aromatic hydrocarbons (6).

The carcinogenicity of these compounds was found to be dependent on the size of the alkyl substituents as well as on the position of the substituent. Usually carcinogenicity decreases as the size of the alkyl substituent increases, for example, the higher homologs of 3-alkylcholanthrenes (1) (2)

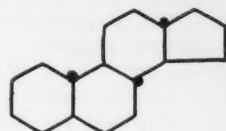


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and 8-alkylbenzanthracenes (7) are less carcinogenic than the corresponding methyl derivatives. There seems to be no definite rule governing the relative carcinogenicity of these hydrocarbons with respect to the position of the alkyl group; for example, among the methylbenzanthracenes, 7-methylbenzanthracene is strongly carcinogenic, 8-methyl followed by 12-methyl derivative is quite carcinogenic, whereas other methyl derivatives are about as ineffective as the parent compound (8). The increase in carcinogenicity of 7- and 12-methylbenzanthracene may be interpreted by an increase in electronic effect due to the introduction of a methyl group into the meso positions (9), but the carcinogenicity of the 8-methyl derivative cannot be accounted for. It is well known that the electronic effect of a methyl group substituted in an aromatic or unsaturated system is very similar to that of an ethyl group, while the latter is virtually indistinguishable from its higher homologs (10). Since all previous correlations were based on the electronic properties of the hydrocarbons, it is not surprising that these attempts failed in the case of alkylated polynuclear aromatic hydrocarbons.

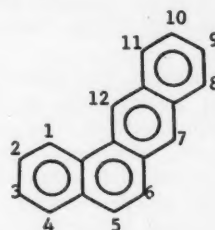
Most carcinogenic polynuclear aromatic hydrocarbons contain four to five condensed aromatic nuclei, and their structural similarity to steroids has been noted (6). Steroids may be converted under drastic conditions to a number of polynuclear aromatic hydrocarbons, among which are the noncarcinogenic Diel's hydrocarbon and the highly carcinogenic 3-methylcholanthrene. Numerous efforts to effect such a conversion in vivo have been unsuccessful.

By careful examination of the Stuart-Briegleb molecular model (11) of various carcinogenic hydrocarbons and steroids, we observed a remarkable resemblance between these two classes of compounds. There is usually a direct increase in carcinogenicity as the hydrocarbons become sterically more similar to steroids. Some of these results are illustrated in Figs. 1-4. In Fig. 1 the molecular model of norandrostane (II)



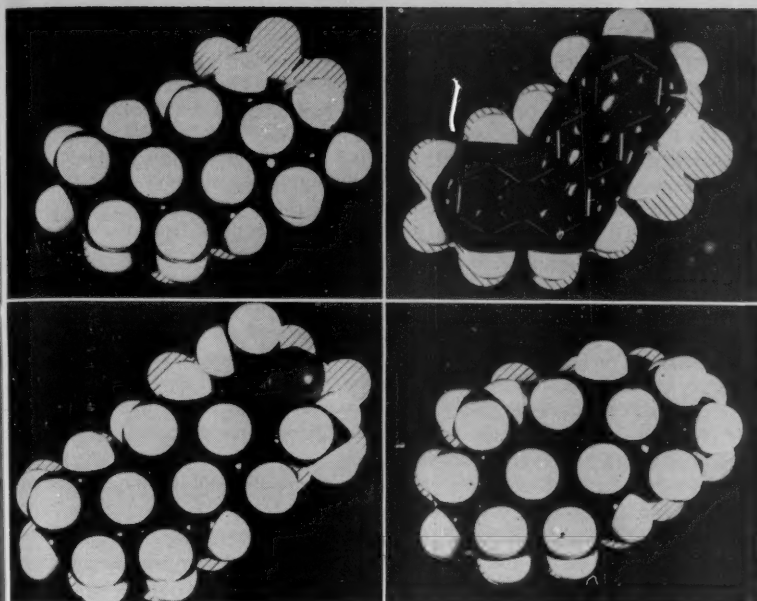
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is compared with that of benzantracene (III);

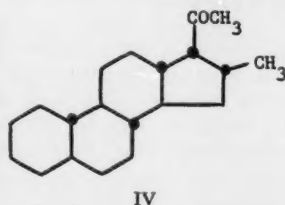


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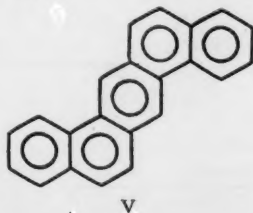
there is a discrepancy near the top of the molecule which may be easily compensated if the 17 position of norandrostane is substituted by a hydroxyl or an acetyl group as in most steroid hormones. In Fig. 2, the molecular model of benzantracene is compared with that of norandrostane; there is a discrepancy at the positions equivalent to C<sub>15</sub> and C<sub>16</sub> of steroids. Introduction of a methyl group to either 7 or 8 position of benzantracene will decrease this discrepancy. 7,8-Dimethylbenzantracene and cholanthrene, which have the same molecular dimension as that of steroids, are among the most potent carcinogens known. 7- or 8-Methylbenzantracene, which is sterically more similar to steroids than the parent hydrocarbon, is also much more carcinogenic. The introduction of higher alkyl groups into benzantracene or cholanthrene will cause the molecule to deviate sterically from steroids; therefore, the higher alkylated hydrocarbons are less carcinogenic, as observed in the homologs of 8-alkylbenzantracene (7) and 3-alkylcholanthrene (2). In Fig 3, the molecular model of 16-methyl-17-acetylnorandrostane (IV),



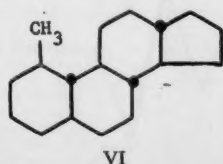
Figs. 1-4. Fig. 1 (top left). Norandrostane versus benzantracene. Fig. 2 (top right). Benzantracene versus norandrostane. Fig. 3 (bottom left). 16-Methyl-17-acetylnorandrostane versus 1,2,5,6-dibenzantracene. Fig. 4 (bottom right). 1-Methylnorandrostane versus benzpyrene.



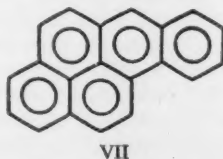
the basic carbon skeleton of a group of biologically active steroids (12), is compared with that of 1,2,5,6-dibenzantracene (V);



in Fig. 4, the molecular model of 1-methylnorandrostane (VI),



the basic carbon skeleton of another group of active steroids (13) is compared with that of benzpyrene (VII).



In either case, remarkable similarity is found. Similar comparisons between all known carcinogenic polynuclear aromatic hydrocarbons and steroids were made.

Our observation suggests that, in addition to the electronic factors, there is a steric factor responsible for the carcinogenicity of the polynuclear aromatic hydrocarbons. For a polynuclear aromatic hydrocarbon to be carcinogenic, it must bear steric resemblance to an active steroid. Among polynuclear aromatic hydrocarbons of similar electronic properties, the closer the steric resemblance to a steroid, the higher is the carcinogenicity.

Because polynuclear aromatic hydrocarbons are devoid of polar functions, such as -OH or -NH<sub>2</sub> groups, the only possible bonding of such compounds to biological systems is that of charge-transfer complex formation. Some interesting correlations have been made between the ability of charge-transfer complex formation of these compounds and the carcinogenicity (5). Since the steric factor

is a requirement for carcinogenicity, one possible implication is that the polynuclear aromatic hydrocarbons may act at the same sites as steroid hormones. Carcinogenesis by these hydrocarbons may be the result of their interference with normal steroid functions. This hypothesis is in agreement with several isolated biological observations, among which are the variation of carcinogenicity of these hydrocarbons by concurrent administration of steroid hormones with these hydrocarbons (14) and the induction of identical morphological changes by some of these hydrocarbons as by progesterone on breast tissue of experimental animals (15, 16).

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## "Conditioned" Alpha Desynchronization

**Abstract.** Results casting doubt on the reported findings of Wells and Wolff on conditioned alpha desynchronization are presented. The experimental findings indicate that these authors were most likely dealing with the phenomenon of adaptation to a complex stimulus. These results are compared to similar phenomena in the conditioning of the galvanic skin response.

In a recent article Wells and Wolff (1) speak of the development of conditioned cerebral responses which were "considered to have occurred when the alpha rhythm was obliterated or strikingly depressed following the presentation of the tone and before the appearance of the light." In view of the results obtained by Knott and Henry in 1941 (2) and by Wells and Wolff (3), we seriously question whether the latter authors demonstrated development of a conditioned cerebral response in their more recent report (1).

We replicated the experimental conditions described by Wells and Wolff, the only difference being the presentation of tone through a speaker rather than through earphones. "Conditioning" consisted of the presentation of a tone (500 cy/sec approximately 40 db above level of audibility) for 4 sec, with light stimulation during the last 3 sec of tone. In our experiment 12 naive subjects were presented with 20 trials of tone stimulation (adaptation) prior to the 50 conditioning trials. The results of only ten subjects could be used, two subjects showing consistent tendencies to drift off into dreamland that could not be checked by instructions for them to remain relaxed but awake.

Alterations in alpha activity (bipolar parieto-occipital leads) were evaluated during the 1 sec of tone stimulation and during the first second of tone coupled with photic stimulation. In all cases alpha activity was compared with that observed during the second preceding the start of tone stimulation. Alpha desynchronization was recorded if amplitude of alpha activity during stimulation fell below that during the preceding period, or if alpha desynchronization (LVF) appeared, or if both occurred. Alpha enhancement was tallied if the amplitude of alpha activity was enhanced during stimulation or if during stimulation alpha activity appeared against a back-

ground of either low voltage fast (LVF) or "drowsy" activity.

Figure 1 shows the results of this experiment. Twenty trials of tone stimulation produce some adaptation of the alpha desynchronization response, although adaptation is far from perfect at this time. If trials demonstrating alpha enhancement are excluded from the analysis, 69 percent of the first five trials show desynchronization, 58 percent during trials 6 to 10, 54 percent during trials 11 to 15, and 45 percent still show desynchronization during the last five trials. The greater degree of desynchronization found in this experiment than in the work of Knott and Henry (2) is attributed to the higher intensity of tone stimulation used in the present experiment. Knott and Henry used a tone just above the auditory threshold of their subjects. Wells and Wolff presented no data on the adaptation portion of their experiment, except for the statement that tone was "repeatedly presented until at least five successive tone presentations failed to suppress alpha activity."

When tone and light are paired we observe enhanced alpha desynchronization during the first five trials (as compared with the last five adaptation trials). The "conditioning" curve, however, looks more like an adaptation than a conditioning curve. There is a

relatively consistent drop in the alpha desynchronization response to tone going from early to later trials. Additional evidence in support of the view that this response is an adaptation response to a new stimulus complex (tone and light as compared with tone alone) is obtained from the curve depicting the response to light stimulation, to which some adaptation also occurs. The two curves are identical in inflection nine out of ten times, that is, as one curve goes down so does the other, as one goes up so does the other. Since the response to light is the unconditioned response, a decrease of which can only be attributed to adaptation, it would appear more parsimonious to refer to the changes in alpha desynchronization during "conditioning" as adaptation to a new stimulus complex. The results of recent studies on galvanic skin response conditioning by Stewart *et al.* (4) and Stern *et al.* (5), demonstrating a return of the adapted-out response when it is paired with a new stimulus, would thus also hold for alpha desynchronization conditioning. Knott and Henry have referred to this phenomenon as "sensitization," while the latter authors have referred to it as the return of the "orienting response." Insofar as alpha desynchronization can be considered an "orienting response," the results ob-

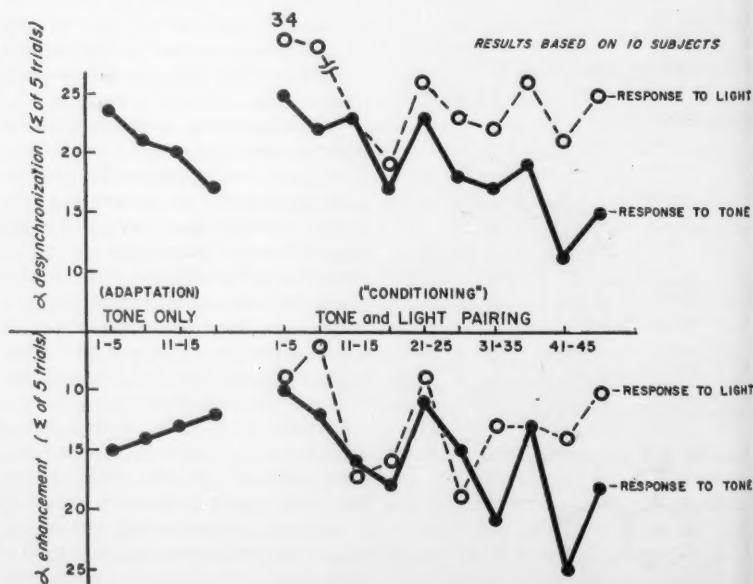


Fig. 1. Effect of tone stimulation and "conditioning" on alpha activity. The upper portion of the graph demonstrates alpha desynchronization in response to stimulation, while the lower portion is for alpha enhancement. (The maximum possible number of responses per unit is 50 to 10 subjects, five trials per subject.)



tained for galvanic skin response "conditioning" are also applicable to alpha conditioning.

If our interpretation of these data is correct, we would predict that if one measured speed of adaptation to tone stimulus alone, one should find that brain-damaged and chronically anxious patients should show adaptation to tone stimulation more rapidly than is true of control subjects. Experiments are presently under way to test this hypothesis.

Analysis of alpha enhancement is depicted in the lower portion of Fig. 1. A rise in the curve is indicative of increasing alertness; a drop, of increasing drowsiness. This interpretation is based on the finding that alpha enhancement or appearance of alpha activity in response to stimulation occurs only in drowsy subjects (6). During the 20 trials of tone stimulation, we see a consistent increase in alertness, while during "conditioning" there is consistent decrease of alertness, or a lapse into a drowsy state, despite instructions on the part of the experimenter aimed at keeping the subject alert and awake. The lack of parallelism between the curves demonstrating alpha enhancement to tone and to light (paired with tone) is attributed to the facts that (i) where there is alerting to tone, further alerting to light is not probable, since the period of analysis for light stimulation immediately follows that of tone stimulation, and (ii) since light is a more potent stimulus for producing alpha desynchronization, it is thus possible for a person to go from a drowsy record to an alert one with minimum or no evidence of alpha activity.

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5 April 1961

11 AUGUST 1961

## New Arrangement of Interrenal and Chromaffin Tissues of Teleost Fishes

**Abstract.** An unusual morphologic arrangement of interrenal and chromaffin tissues has been observed in two families of teleost fishes. In most teleosts in which these cell types occur together in association with the postcardinal veins and their branches, the chromaffin cells are located between the lumen of the vein and the interrenal cells. This typical relationship is reversed in some of the Labridae and Scaridae.

The interrenal gland of teleost fishes, located within the anterior or head kidney, appears to be homologous to the adrenal cortex of mammals (1, 2). Chromaffin cells like those of the adrenal medulla, which react with chromic acid, are also found in the anterior kidney. These cell types were delineated first by Giacomini in 1902 (3); since then the interrenal and chromaffin tissues of about 80 species of teleosts have been described (1, 4, 5).

In order to extend these observations, over 125 species from 55 teleost families were collected from a variety of habitats (6). The anterior kidneys of these animals were fixed either in Bouin's or in Orth's (7) fluid. The latter fixative contains potassium dichromate, and was used to determine the distribution of chromaffin cells.

The interrenal morphology is extremely variable in these fishes. Furthermore, the surrounding tissues may be lymphoid or myeloid or both, and may or may not contain renal elements (2). The relationship of the interrenal to these tissues is also variable. Usually the interrenal is associated with the postcardinal veins or their branches or both, which ramify through the anterior kidney tissue. Chromaffin cells are always located within the walls of these veins. Often the interrenal and chromaffin tissues are separate, although more frequently there is some type of association between them.

When interrenal and chromaffin cells occur together around the veins within the anterior kidney, one of several possible arrangements may be found. The chromaffin tissue may be interspersed among the interrenal cells, as in the Cyprinidae and Cyprinodontidae (5). In the Gasterosteidae (5), clumps of interrenal alternate with clumps of chromaffin cells, the entire complex forming a cuff around the lumen of the postcardinal vein.

More often only the chromaffin cells are seen within the walls of these veins, either adjacent to the endothelium or embedded within the connective tissue of the vein wall. The interrenal is found external to both the vein wall and its associated chromaffin tissue. Such an arrangement is illustrated in Fig. 1 (A, B), which shows the interrenal and chromaffin tissue of a butterfly fish, *Chaetodon miliaris*. Even in the truly interspersed glands mentioned above, the chromaffin cells tend to be located closest to the vein lumen.

During the course of this investigation, an unusual arrangement of the interrenal and chromaffin tissues was seen. This arrangement has not been described previously, and has been observed only in fish from two closely related families: the Labridae (wrasses) and the Scaridae (parrot fishes). In some of these animals, the interrenal cells were found immediately adjacent to the endothelium of the veins, as a single layer of columnar cells. The

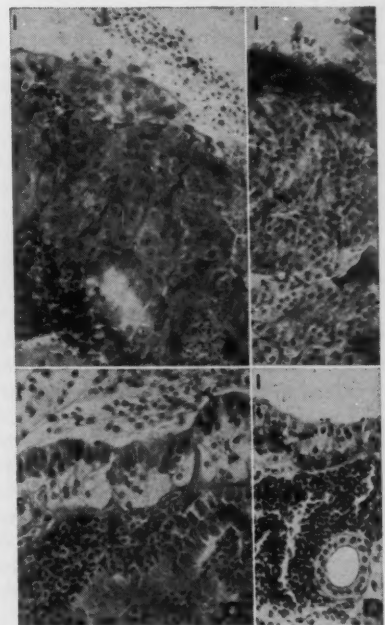


Fig. 1. Interrenal and chromaffin tissues associated with a branch of the postcardinal vein within the anterior kidney. Tissues were stained with hematoxylin and eosin; magnification is  $\times 365$ . (A) *Chaetodon miliaris*, Bouin's fixation. (B) *Chaetodon miliaris*, Orth's fixation. (C) *Cheilinus rhodochrous*, Bouin's fixation. (D) *Cheilinus rhodochrous*, Orth's fixation. Abbreviations: i, interrenal cells; c, chromaffin cells (the positively reacting chromaffin cells appear dark after Orth's fixation); l, vein lumen.

chromaffin cells lie between the interrenal and the connective tissue of the vein wall (Fig. 1, C, D). This peculiar arrangement of cells was observed in all of the species of Scaridae examined, which included *Scarus dubius*, *S. formosus*, *S. perspicillatus*, and *Scarops rubroviolaceus*. In regions of the anterior kidney where the interrenal is markedly thickened, however, the interrenal and chromaffin cells were often interspersed.

Among the Labridae studied, the relationship between interrenal and chromaffin cells illustrated in Fig. 1 (C, D) was seen in the following species: *Cheilinus rhodochrous* (Fig. 1, C, D), *Cheilio inermis*, *Hemipteronotus baldwini*, *Novaculichthys taeniourus*, *N. woodi*, *Thalassoma duperreyi*, and *T. umbrostigma*. In most of these fishes, other arrangements were also seen, especially in those regions where the interrenal cells are stratified. In five other species of Labridae (*Bodianus bilunulatus*, *Coris flavovittata*, *C. ballieui*, *Cymolutes leclusei*, *Thalassoma ballieui*), this unusual relationship of interrenal and chromaffin cells was not observed.

Modifications of interrenal location and morphology may be related to the maintenance of an adequate blood supply to this gland, particularly as it increases in size. The function of the sinusoids visible in the interrenal of *Chaetodon* (Fig. 1A) may be performed by the larger blood vessel in *Cheilinus* (Fig. 1C), as long as only a single layer of interrenal cells lies adjacent to the vein lumen. It is noteworthy that the chromaffin cells maintain a relatively constant position in the vein wall despite marked variations in the distribution of interrenal tissue. The significance of these morphologic variations is not apparent, and attempts to correlate interrenal structure with habitat or taxonomic position of the species have thus far been unsuccessful (8).

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8. I am indebted to Howard A. Bern for his advice during the course of this study, as well as for his help in the collection of much of the material. I thank Lillian Pissott and David Stiller for making many of the histologic preparations, and Victor Duran for the photomicrography. This study was aided by National Science Foundation grant G-8805 and U.S. Public Health Service grant CRT-5045, and by a predoctoral fellowship from the National Science Foundation. This study is contribution No. 157 from the Hawaii Marine Laboratory.

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### Potassium Deficiency in Marmots during Hibernation

**Abstract.** Semiquantitation of potassium deficiency in the renal papillae indicates that woodchucks (*Marmota monax*) are deficient in potassium annually during the time they subsist on stored fats. The deficiency begins prior to hibernation, progresses during hibernation, and, in males, continues during the immediate post-emergence period.

A deficiency of potassium appears to be a regular annual event in woodchucks (*Marmota monax*). The deficiency begins prior to hibernation and reaches a maximum immediately after hibernation. During this part of the year the animals subsist on stored fats rather than on ingested food.

Potassium deficiency in these animals is shown by the presence in the cells of the tips of the renal papillae, especially of the collecting tubules, of PAS positive intracytoplasmic granules, or drop-

lets, identical to those which result from potassium deficiency in laboratory rodents (1-3). These droplets alone are presumptive evidence of a potassium deficit (3). However, the fact that the degree of granulation in woodchucks correlates with serum potassium levels establishes the identity of the droplets as being those produced by a potassium deficit. This relationship permits the use of papillary granulation as an index of potassium deficiency and roughly of its relative degree and duration.

The kidneys of about 2000 woodchucks from the Letterkenny Army Ordnance Depot near Chambersburg, Pa., were examined from 1956 through 1960. Sections through the tips of the renal papillae, cut at 3  $\mu$  and stained by Lillie's allochrome procedure (4), were available for about 1000 of these (Table 1). The degree of granule formation was graded for each kidney on a scale of 0 to 4, in which 0 indicated no granules and 4 corresponded to the marked degree of granulation observed in rats made severely deficient in potassium experimentally (1).

Animals were collected in all months but January and the first half of February, although samples were necessarily small in the months immediately preceding and during hibernation (Table 1). Both males and females begin hibernation in October in the study area. The midpoint of emergence from hibernation is 22 February for adult males and 5 March for adult females. Two torpid animals were taken from underground burrows in December (Table 1). More animals from December and January would be desirable, but woodchucks are difficult to locate in their burrows during hibernation. Serum potassium levels were determined for a

Table 1. Mean grade of PAS positive granulation in epithelial cells of the collecting ducts of the renal papillae of woodchucks. Grading based on a scale of 0 to 4, where 0 = no granules and 4 = the granulation seen in severe experimental potassium deficiency in rats. Data are combined for 1956 through 1960. *P* differences are as follows: between males and females in February, <0.05; between males and females in March, <0.001; between males for February/March and March/April, <0.001; between females for February/March, <0.05; between females for March/April, <0.02; between males for April/May, <0.05. Differences between all other paired successive means: no significance.

Month	Males			Females			Sexes combined		
	No.	Mean	S.E.	No.	Mean	S.E.	No.	Mean	S.E.
February	30	3.47	0.14	4	2.50	0.41			
March	139	2.23	.12	108	1.58	.12			
April	121	1.33	.12	152	1.20	.10	273	1.26	0.07
May	25	0.84	.21	54	0.68	.11	79	0.73	.10
June	32	0.48	.16	45	0.54	.14	77	0.52	.11
July	32	0.61	.27	78	0.40	.07	110	0.46	.08
August	7	0.57	.28	21	0.48	.15	28	0.50	.13
September	45	0.74	.15	51	0.81	.18	96	0.78	.11
October	10	0.95	.34	5	0.80	.34	15	0.90	.25
November	3	1.00	.58	5	1.00	.71	7	1.00	.44
December	1	2.00		1	3.00		2	2.50	

	DEGREE OF PAPILLARY GRANULATION				
	0	1	2	3	4
No. ♂	18	19	14	14	6
No. ♀	65	28	21	15	3

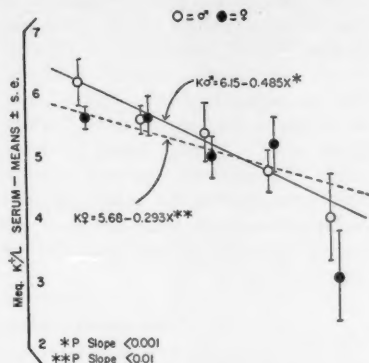


Fig. 1. Degree of granulation in the renal papillae on a basis of 0 to 4 plotted against serum potassium levels for 71 male and 132 female woodchucks.

random sample of 346 animals (5). Comparisons between serum potassium and degree of granulation were possible for 203 of these for which there were sections through the papillary tips. Muscle potassium was not measured.

Serum potassium levels declined significantly as the degree of granulation increased in both sexes (Fig. 1). However, the relationship was poorer in the females, as indicated by the lower slope and lower degree of significance, in spite of a much larger sample size. The adjusted mean serum potassium levels of the two regressions were not different (5.15 for males and 5.45 for females), but the difference between the slopes approached significance ( $P < 0.10$ ). Pregnancy and lactation may account for the greater variability in the females. Nevertheless, use of the degree of papillary granulation as a rough index of the degree of potassium deficiency is justified by the significant correlation between papillary granulation and serum potassium levels in both cases.

Renal papillary granulation is marked when the woodchucks emerge from hibernation (Table 1). It then declines exponentially through June, remains at a low level through August, and begins to increase again to reach a relatively marked degree by December (Table 1). The pattern of change in the degree of granulation throughout the year was the same for every year, from 1956 through 1960. During February and March the degree of granulation is significantly greater in males than it is in females

(Table 1), but by April the values for both sexes were the same. These differences are accounted for by the fact that males begin to emerge from hibernation about a month before the females, although the mid-points of emergence are about 2 weeks apart. During this period there is little or no food available, and the gastrointestinal tracts of the males invariably are empty (6). Consequently, the males are living entirely on stored fat then and, to a lesser extent, afterwards (6). On the other hand, the females emerge at about the time food becomes available. The greater degree of granulation and, therefore, presumably, potassium deficiency in males apparently is due to continuing potassium losses without dietary repletion during the 2 to 4 weeks immediately following hibernation. On the other hand, it is clear that the granulation begins to develop immediately prior to hibernation and continues to progress during, and particularly after, hibernation when the animals again are depending on stored fat without ingesting food and, consequently, potassium.

From the preceding evidence, it appears that woodchucks experience an uncompensated loss of potassium during the period of the year in which they subsist largely on stored fats; that is, immediately prior to and during hibernation and, for males, during the immediate postemergence periods. The loss apparently is progressive and cumulative until repletion begins early in March. The loss of potassium could be aggravated by a relatively increased activity of sodium and water-retaining endocrine mechanisms, such as a relative increase in aldosterone secretion, during hibernation. However, this aspect of the problem has not been explored. The adrenal glands in these animals weighed the least during hibernation and increased in weight every year from the end of hibernation until June, apparently as a result of stimulation by social factors (unpublished data). So changes in adrenal weight correlate negatively with the degree of papillary granulation and serum potassium levels. The significance of this relationship, if any, is not apparent.

The rate of potassium repletion, in terms of the disappearance of specific granulation, appears to occur at a constant rate, as indicated by the data in Table 1. Degranulation follows closely a negative exponential curve for each year.

Based on the above evidence it would

appear that the development of a relative potassium deficit is a regular feature of hibernation in woodchucks, brought about by continuing losses of potassium without dietary replenishment during the period of dependence on stored fats (7).

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#### Existence of Absorption Bands at 730-740 and 750-760 Millimicrons in Algae of Different Divisions

**Abstract.** Absorption studies, made on suspensions of *Anacystis nidulans*, *Chlorella pyrenoidosa*, and *Porphyridium cruentum* by means of an integrating spectrophotometer, suggest the existence of pigments absorbing "extreme red" light in the 720- to 800-m $\mu$  region. In the blue-green alga *Anacystis*, one pigment of this type exists, which produces a relatively strong absorption band at 750 m $\mu$ . In the green alga *Chlorella* and the red alga *Porphyridium*, two considerably weaker absorption bands appear, at 730 to 740 m $\mu$  and 750 to 760 m $\mu$ , which may be due to one or two pigments. These pigments must be responsible for the photoinhibition of photosynthesis observed in these algae in the same spectral region; as yet, no photoinhibition has been observed in *Anacystis*.

Rabinowitch *et al.* (1) and Govindjee *et al.* (2, 3) have demonstrated the occurrence of photoinhibition of both photosynthesis and the Hill reaction by extreme red light in various algae. This caused us to make a search for the presence in algal cells of pigments absorbing in the extreme red region of the spectrum. The green alga *Chlorella pyrenoidosa*, the red alga *Porphyridium cruentum*, and the blue-green alga *Anacystis nidulans* were used. *Chlorella* and *Porphyridium* were grown as previously described (see 4); *Anacystis* is now be-



ing grown in our laboratory in the "standard nitrate" medium developed by Emerson and Chalmers for the growing

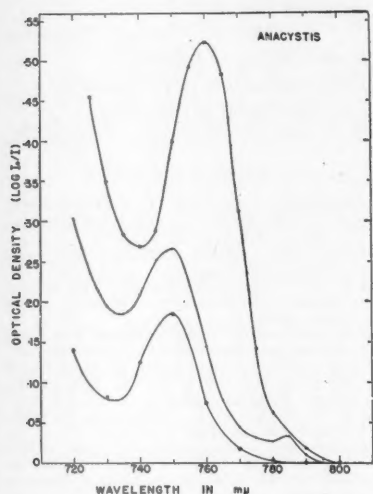


Fig. 1. Absorption spectra of thick suspensions of *Anacystis nidulans* showing the occurrence of pigment "P750" in three cultures of different density.

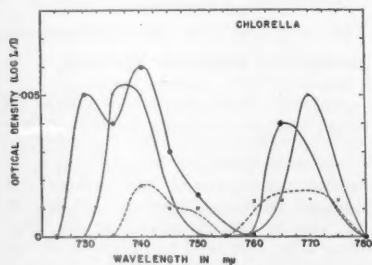


Fig. 2. Absorption spectra of thick suspensions of *Chlorella pyrenoidosa* show the existence of pigments "P740" and "P760" in three different cultures.

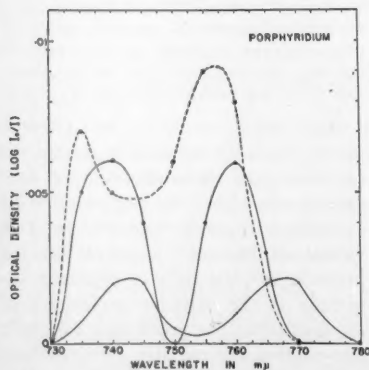


Fig. 3. Absorption spectra of thick suspensions of *Porphyridium cruentum* showing the existence of pigments "P740" and "P760" in three different cultures.

of *Chlorella* (unpublished). We prefer this completely inorganic medium to the citrate-containing medium used by Kratz and Myers (5).

The algal cultures were centrifuged and resuspended, either in their culture medium or in an appropriate carbonate-bicarbonate buffer. The bands were first noted as weak but reproducible wiggles on the absorption curves obtained by the usual methods. Because of their weakness, measurements were made on very thick suspensions, with optical densities of about 2.0 at 680 mμ. In making measurements at low optical densities in very concentrated suspensions, both the stability of the instrument and the accuracy with which it can measure true absorption in a strongly scattering suspension are important. Of the instruments available to us, our 12-cell integrating spectrophotometer (6) comes closest to satisfying these requirements. Readings were taken at 5-mμ intervals; the half-intensity band width was 2.0 mμ.

Suspensions of *Anacystis* revealed clearly the presence of an absorption peak at 750 mμ (Fig. 1), which has been mentioned earlier (2). In some experiments with this alga, the peak was found at 760 mμ; the cause of this difference is unknown. The presence of a 750-mμ pigment ("P750") in *Anacystis* can be detected also with the Beckman DU spectrophotometer. Contrary to what one would expect from the relatively high intensity of this absorption band, *Anacystis* is the one algal species in which no photoinhibition effect could be noted (2).

Absorption spectra of several suspensions of *Chlorella* and *Porphyridium* (prepared from different cultures) showed two absorption bands in the extreme red, at 730 to 740 mμ and at 750 to 760 mμ, respectively. Figures 2 and 3, obtained by correcting the experimental absorption curves for a "tail" of the chlorophyll *a* absorption band (assumed to fade out smoothly on the long-wave side), clearly show the two new bands.

We believe that the pigments ("P740 + P760") producing these absorption bands are responsible for the inhibition effect previously detected in photosynthesis and in the Hill reaction of the same algae, since these absorption peaks coincide with the peaks observed in the action spectrum of inhibition (3). The weakness of the absorption bands shown in Figs. 2 and 3 suggests that the pig-

ments are either present in very low concentrations or have very low extinction coefficients.

No evidence has yet been obtained of the chemical nature of the new pigments ("P750" and "P740 + P760"). Some experiments suggest, however, that the pigment "P740 + P760" may be similar to the "phytochrome," which Butler *et al.* (7) have found in higher plants. Alternatively, the new absorption bands could be due to microcrystals of the chlorophylls, since the latter are known to absorb in the same spectral region (8, 9).

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9. We are grateful to J. B. Thomas for his interest in this investigation. Thanks also are due to Rajni Govindjee for her assistance. We take pleasure in acknowledging financial support from the National Science Foundation and the U.S. Public Health Service.

7 March 1961

#### Air Entrainment in Turbulent Liquids

**Abstract.** An experimental technique has been developed for measuring the concentration and distribution of air entrained by turbulence in an agitated liquid. The air content was related to the viscosity, surface tension, and turbulence of the liquid by dimensional analysis.

The concentration and distribution of air in turbulent water have been measured by several investigators both by mechanical sampling (1) and by electrical methods (2) in laboratory channels set at slopes sufficiently steep that when the turbulent boundary layer intersected the free surface there was sufficient transverse kinetic energy to overcome the stabilizing effects of surface tension and air was entrained into the water. The air bubbles were then



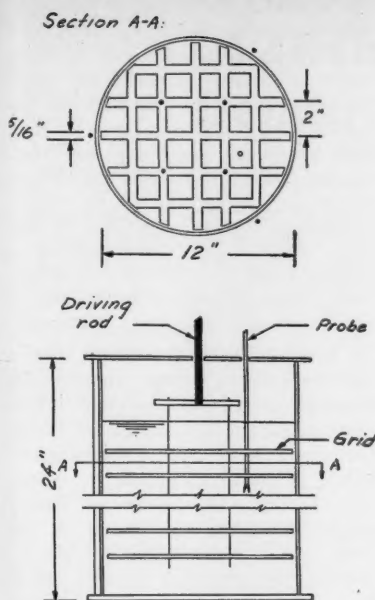


Fig. 1. Grid agitator used to generate homogenous turbulence in a liquid. The driving rod is connected to an eccentric on a variable-speed drive.

carried to some depth in the water by the mechanism of turbulent diffusion.

This report summarizes the results of an experimental study of the mechanism of air entrainment as it is related to significant fluid properties and to turbulence artificially induced by a moving grid in a container of liquid. The surface tension, viscosity, and density of the liquid determine the

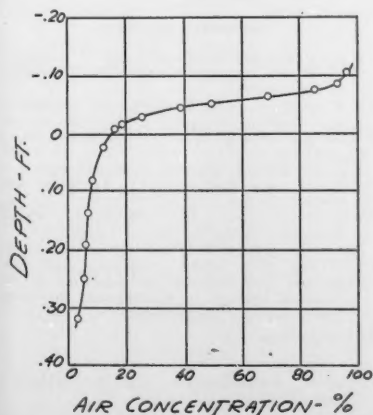


Fig. 2. Typical distribution of air entrained into water through the free surface by turbulence. Negative values of depth result from bulking of the air-water mixture.

amount of air entrained and the size and concentration of the air bubbles within the liquid for any given degree of turbulence. This interrelationship can be expressed as

$$C = \phi(\epsilon, \rho, \mu, \sigma, \gamma) \quad (1)$$

where  $C$  is the mean air content by percent of volume in the container,  $\epsilon$  is the diffusion coefficient,  $\rho$  is the density,  $\mu$  is the viscosity,  $\sigma$  is the surface tension, and  $\gamma$  is the specific weight of the liquid.

The turbulence was generated by a grid agitator moving vertically in simple harmonic motion in a transparent container of the liquid (see Fig. 1). The amplitude and frequency of the stroke and the geometry of the agitator were varied. The liquids used were water, ethyl alcohol, methyl alcohol, and sugar-water solutions at different temperatures. These liquids permitted significant changes in the fluid properties. An electrical probe similar to that developed by Lamb and Killen (2) was used to measure the concentration of air at any level. A typical distribution of the air is shown in Fig. 2.

Since the eddy coefficient cannot be readily evaluated, the dimensional analysis of the problem proceeded from the following relationship

$$C = \phi'(v, l, d, \rho, \mu, \sigma, \gamma) \quad (2)$$

where the diffusion coefficient ( $\epsilon$ ) of Eq. 1 has been replaced by  $v$ , the mean velocity,  $l$ , the stroke, and  $d$ , the grid spacing of the agitator.

Application of the  $\pi$  theorem resulted in the following relationship

$$C = \phi''\left(\frac{l}{d}, \frac{v\rho}{\mu}, \frac{v^2\rho l}{\sigma}, \frac{lg}{v^3}\right) \quad (3)$$

where the first term in parentheses is a dimensionless geometry parameter and the remaining terms are forms of the familiar Reynolds ( $R$ ), Weber ( $W$ ), and Froude ( $F$ ) numbers.

Equation 3 was evaluated from results of these tests to be

$$C = 0.013 (R^{0.21} W^{0.22} F^0)$$

The exponent of the Froude number averaged near zero, indicating that gravity has a negligible effect on air entrainment for the liquids tested.

Visual observation of the entrainment process indicates that entrainment occurs when the surface undulations form breaking waves. Then turbulent mixing carries the air bubbles deep

into the liquid. Decreasing the surface tension results in greater surface action and greater air entrainment; similarly, the greater the turbulence, the greater the air entrainment. Decreasing the viscosity permits more bubbles to be carried into the fluid (3).

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JOHN H. NATH\*

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University of Colorado, Boulder

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- \* Present address: Department of Civil Engineering, Colorado State University, Fort Collins.

6 April 1961

#### Pre-Columbian Littorina littorea in Nova Scotia

**Abstract.** *Littorina littorea*, an abundant northeast North American gastropod, was thought to have been introduced from Europe about 1840. Shells of that species found in ancient Micmac Indian camp sites in Nova Scotia have been radiocarbon-dated as pre-Columbian. Failure of *L. littorea* to extend its range southward before 1840 may have been due to oceanographic factors.

*Littorina littorea* (Linn.) is probably the most abundant intertidal gastropod occurring between the Gulf of St. Lawrence and southern New Jersey. Long native in Europe from the White Sea to Gibraltar and in the British Isles (1), it was first recorded from North America about 1857 when Willis reported it from Halifax, Nova Scotia (see 2). Its subsequent progressive colonization of more southerly localities has been well documented by Morse (3), who states that it first occurred at Portland and Kennebec, Maine, in 1870; at Salem and Provincetown, Massachusetts, in 1872; at Woods Hole, Massachusetts, in 1875; and at New Haven, Connecticut, in 1880. Morse also stated (3) that he had received specimens from Bathurst, Bay of Chaleur, Gulf of St. Lawrence, in 1855, and Dawson (see 2) reported that he had collected it at Pictou on

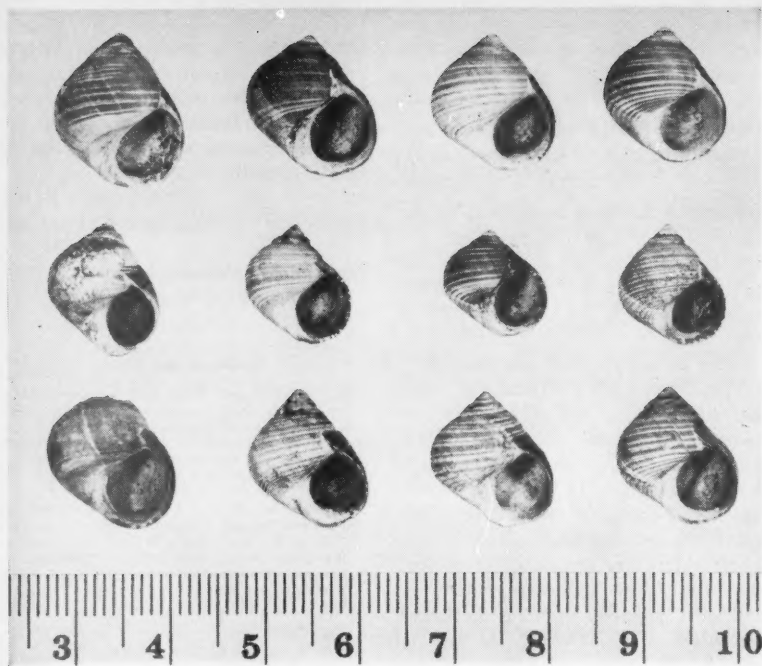


Fig. 1. *Littorina littorea* from Reid Site, Indian Point, St. Margaret's Bay, Halifax County, Nova Scotia (scale is in centimeters).

Northumberland Strait, Nova Scotia, in 1840 and believed that because of its wide distribution it was "a regular and probably aboriginal member of the fauna of Acadia." Because of the rapid southward spread of the species shortly after its discovery, modern workers (1) have discounted Dawson's views and accepted Ganong's theory (2) that *L. littorea* was introduced to the Halifax region about 1840 by commerce and that its southward spread was a direct result of that introduction.

During the summer of 1960, one of us (J.S.E.) was engaged in archeologic investigations of Micmac Indian camp sites (4) near Halifax, Nova Scotia. At Reid Site, Sand Cove, and at Frostfish Cove (both at Indian Point, St. Margaret's Bay, Halifax County), specimens of *Littorina littorea* were found among undisturbed hearth debris and were associated with *Cepaea hortensis* (Müller), other shells, bones, charcoal, and prehistoric artifacts. The only artifacts in the site of later origin were

rusty, wrought-iron nails in a line that probably had once been a rail fence. The valves of *Mercenaria mercenaria* (Linn.) which were present were unusually thick and exhibited crowded lines of growth, conditions which normally indicate a cold environment close to the lower limit of tolerance for *M. mercenaria* (5). Reindeer (*Rangifer tarandus*) bones, absent from older deposits, were also found and provided further evidence that the climate had been cold and was becoming colder. From this information a date corresponding to the latter stages of the Little Ice Age was tentatively assigned—that is, the 13th century.

Radiocarbon dating of 12 of the *Littorina littorea* shells from Reid Site gave an age of  $700 \pm 225$  yr B.P. (6) and showed that the original estimate of age was approximately correct.

The specimens which were submitted for dating are shown in Fig. 1. Their dimensions are apparent in the figure. A 13th specimen, which was

not submitted for dating, measured as follows: height, 16.6 mm; width, 15.0 mm; whorls, four and a half; aperture length, 12.8 mm; and aperture width, 9.5 mm. The specimens show no essential divergence in pattern or form from specimens now living near Halifax or elsewhere within the North American range of the species. Figure 1 indicates that the population is normally variable and implies no lack of genetic diversity.

The conclusion that *Littorina littorea* was native to the Halifax area before the advent of European culture appears well founded. It is also probable that Dawson was correct and that *L. littorea* may have occurred in the Northumberland Strait area, a region which today supports a distinctive warm-water fauna. Its failure to spread southward before the middle of the 19th century may have been the result of oceanographic factors. Drift-bottle studies (7) indicate that the major surface circulation on the Nova Scotian shelf is such that pelagic eggs and larvae of *L. littorea* spawned in the Halifax area would probably be carried out to sea and perish. It appears likely, then, that increased commerce between Halifax and one or more ports in southwest Nova Scotia or New England caused the species to colonize areas, just prior to 1870, from which further extension of its range southward could be mediated by the more favorable long-shore ocean currents which occur in that region (8).

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31 March 1961

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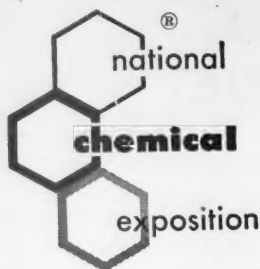
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**Temperature integrator** designed to record storage conditions of frozen food operates on electrochemical principles. The device is about the size and shape of a cigarette. To start its action, the indicator is squeezed to break a capsule of solution inside. The solution connects two dissimilar metal electrodes allowing the electrochemical reaction to start. Progress of the reaction is indicated by change of color

of an indicator paper. The change, from yellow to red, progresses from one electrode to the other. In the present device, the red zone moves the full length of the scale in about 20 days at 20°F, 2 mo at 15°F, 6 mo at 10°F, and in more than 1 yr at 0°F. At 25°F the indicator will travel the full scale in a couple of days. (Minneapolis-Honeywell Regulator Co., Dept. Sci-276, 2747 4th Ave. S., Minneapolis 8, Minn.)

**Event programmer** can schedule up to eight separate events to occur at time intervals which are from 100 msec to 5 sec apart. Provision is made for remote starts and emergency reset is possible at any time. Each time interval is individually set with accuracy said to be  $\pm 5$  percent of dial setting. (Atlantic Research Corp., Dept. Sci-278, Alexandria, Va.)

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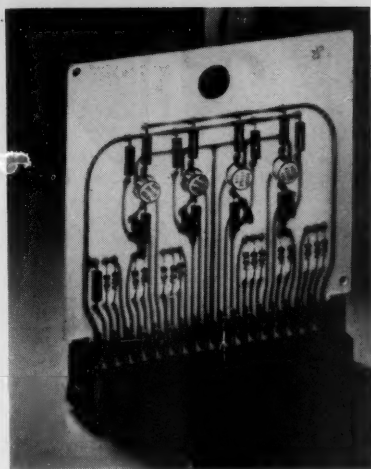


Fig. 1. Digital module.

registers, arithmetic units, or other logical units. Each transistor output can drive ten inputs at rates from 0 to 200 key/sec; standard levels are 0 and -12 volts. Compatible system elements available include clock, relay driver, card cage, and power supply. (Computer Logic Corp., Dept. Sci248, 11800 W. Olympic Blvd., Los Angeles 64 Calif.)

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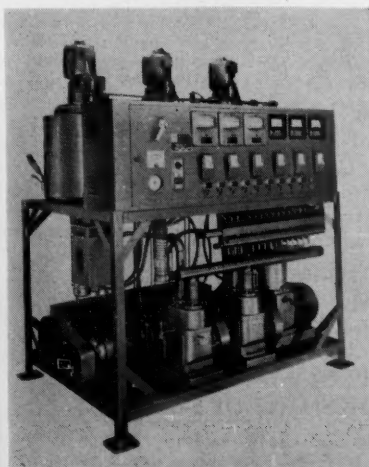


Fig. 2. Molecular still.

**Microwave phase meter** is a direct-reading instrument for the frequency range 300 to 4000 Mcy/sec. Operation of the instrument is based on square-law response to a standing-wave pattern, the pattern being the resultant of the two signals whose relative phase is being measured. Resolution is said to be  $0.1^\circ$  at the microwave frequency. An output is provided for use as an error signal for automatic phase control. The instrument can be adapted for swept-frequency operation with automatic recording. (Wiltron Co., Dept. Sci274, 717 Loma Verde Ave., Palo Alto, Calif.)

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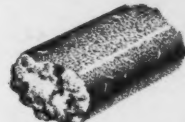
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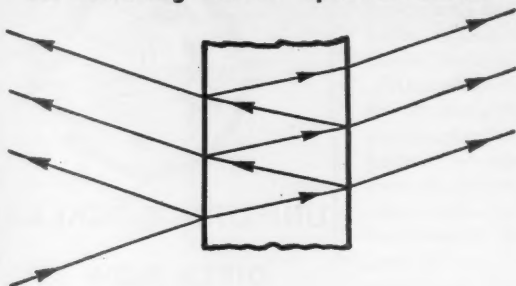
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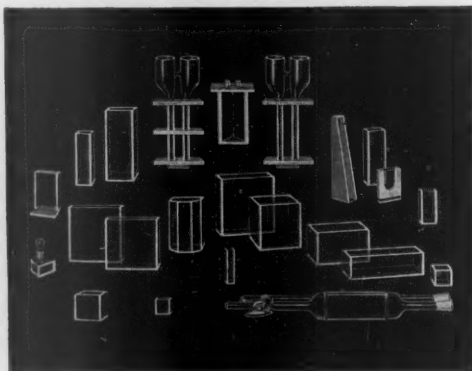
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Editor L. P. Reitz

April 1960

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# Meetings

## Forthcoming Events

### August

30-1. Bionics Symp., 2nd annual, Ithaca, N.Y. (R. Earle, G.E. Advanced Electronics Center, Ithaca)

30-1. Semiconductor Conf., 3rd annual, Los Angeles, Calif. (W. V. Wright, Electro-Optical Systems, Inc., 125 N. Vinedo Ave., Pasadena, Calif.)

30-2. American Sociological Assoc., St. Louis, Mo. (T. Parsons, Dept. of Social Relations, Harvard Univ., Cambridge, Mass.)

30-2. Experimental Research on Shell Structures, colloquium, Delft, Netherlands. (A. L. Bouma, Dept. of Civil Engineering, Technological Univ., Delft)

30-5. Mental Health, 6th intern. congr., Paris, France. (Miss E. M. Thornton, World Federation for Mental Health, 19 Manchester St., London, W.1, England)

30-6. British Assoc. for the Advancement of Science, 123rd meeting, Norwich, England. (Secretary, BAAS, 18 Adam St., London, W.C.2, England)

31-2. Exfoliative Cytology, intern. congr., Vienna, Austria. (Office of the Secretary of the Congress, 666 Elm St., Buffalo 3, N.Y.)

31-2. Gynaecological Cytology, 1st intern. congr., Vienna, Austria. (R. M. Graham, Roswell Park Memorial Inst., 666 Elm St., Buffalo 3, N.Y.)

31-4. Preventive and Social Medicine, meeting, Evian, France. (Société Française de Médecine Préventive et Sociale, 1 rue de Courcelles, Paris 8, France)

31-6. American Psychological Assoc., 69th annual, New York, N.Y. (J. G. Darley, 1333 16th St., NW, Washington 6)

### September

1-5. Danube Research, intern. symp., Budapest, Hungary. (Biological Sciences Group, Hungarian Acad. of Sciences, Roosevelt Tèr. 9, Budapest V)

1-9. Topology and Its Methods in Other Mathematical Disciplines, symp., Prague, Czechoslovakia. (Organizing Committee, Ke Karlovu 3, Prague 2)

1-10. International Pharmaceutical Students' Federation, 7th congr., Munich, Germany. (U. Peto, 10 Groffstr., Munich 19)

2-7. International Assoc. for Quaternary Research, Warsaw, Poland. (R. Galon, Secretary General, INQUA, Geographical Inst. Univ., Torun, Poland)

2-9. International Soc. of Surgery, 19th congr., Dublin, Ireland. (T. C. J. O'Connell, 35 Fitzwilliam Pl., Dublin)

3-7. International Assoc. for Hydraulic Research, 9th congr., Belgrade, Yugoslavia. (H. J. Schoemaker, Waterloopkundig Laboratorium, Raam 61, Delft, Netherlands)

3-8. American Chemical Soc., 140th meeting, Chicago, Ill. (A. T. Windstead, National Meetings Dept., ACS, 1155 16 St., NW, Washington 6)

3-9. International Federation of Gynaecology and Obstetrics, 3rd world congr., Vienna, Austria. (V. Grünberger, Medi-

zinische Akademie, Alserstrasse 4, Vienna 9)

3-10. Inter-American Congr. of Radiology, 7th, São Paulo, Brazil. (W. Bomfim-Pontes, Rua Cesario Motta 112, São Paulo)

4. World Federation for Mental Health, 14th annual, Paris, France. (WFMH, 19 Manchester St., London, W. 1, England)

4-6. International Assoc. for Shell Structures, colloquium, Brussels, Belgium. (Prof. Dutron, 127 Avenue Adolphe Buyl, Brussels 5)

4-6. International Symp. on the Earth Storm, Kyoto, Japan. (T. Nagata, Science Council of Japan, Ueno Park, Tokyo)

4-7. Neuropathology, 4th intern. congr., Munich, Germany. (W. Haymaker, Armed Forces Inst. of Pathology, Walter Reed Army Medical Center, Washington 25)

4-7. Rheumatology, 10th intern. congr., Rome, Italy. (C. B. Ballabio, Clinica Medica Generale, Via F. Sforza 35, Milan, Italy)

4-8. Low Energy Nuclear Physics, intern. conf., Manchester, England. (L. J. B. Goldfarb, Physics Dept., Univ. of Manchester, Manchester)

4-8. Pharmaceutical Sciences, 21st intern. congr., Pisa, Italy. (Intern. Pharmaceutical Federation, 11 Alexanderstraat, The Hague, Netherlands)

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4-8. Plasma Physics and Controlled Nuclear Fusion Research, conf., Salzburg, Austria. (Intern. Atomic Energy Agency, United Nations, New York, N.Y.)

4-9. International Assoc. for Analog Computation, 3rd intern. sessions, Belgrade, Yugoslavia. (D. Strujic, Decanska 14/IV, Belgrade)

4-9. International Congr. of Angiology, 4th, Prague, Czechoslovakia. (Z. Reinis, 4th Medical Clinic, Prague 2/499)

4-9. International Symp. on Fundamental Problems in Turbulence and Their Relation to Geophysics (by invitation), Marseilles, France. (Intern. Union of Geodesy and Geophysics, 53 Avenue de Breteuil, Paris 7)

4-9. Laurentian Hormone Conf., Hoberg's Resort, Lake County, Calif. (Committee on Arrangement of the Laurentian Hormone Conference, 222 Maple Ave., Shrewsbury, Mass.)

4-13. Inter-African Conf. for Food and Nutrition, 4th, Bukavu, Congo Republic. (Commission for Technical Cooperation in Africa South of the Sahara, Pvt. Mail Bag 2359, Lagos, Nigeria)

4-14. Anglo-American Aeronautical Conf., 8th, London, England. (Inst. of Aerospace Sciences, 2 E. 64 St., New York, N.Y.)

5-8. International Congr. of Homeopathic Medicine, 25th, Amsterdam, Netherlands. (J. L. Fonteijn, Westzijde 116, Zaandam, Netherlands)

5-8. Machine Translation of Languages and Applied Language Analysis, intern. conf., Teddington, England. (L. Dostert,

Director, Machine Translation Research, Georgetown Univ., 1715 Massachusetts Ave., NW, Washington 6)

5-8. National Chemical Exposition, 11th, Chicago, Ill. (Chicago Section, American Chemical Soc., 86 E. Randolph St., Chicago 1)

6-8. Effects of Ionizing Radiations on Immune Processes, intern. symp., Lawrence, Kan. (C. A. Leone, Dept. of Zoology, Univ. of Kansas, Lawrence)

6-8. Transmission and Processing of Information, intern. symp., Boston, Mass. (R. M. Fano, Research Laboratory of Electronics, Massachusetts Inst. of Technology, Cambridge 39)

6-12. Human Genetics, 2nd intern. conf., Rome, Italy. (L. Gedda, 5 Piazza Galeno, Rome)

7-8. Pacific Slope Biochemical Conf., annual, San Diego, Calif. (R. G. Wolfe, Chemistry Dept., Univ. of Oregon, Eugene)

7-9. International Cardiovascular Soc., 5th congr., Dublin, Ireland. (H. Haimovici, 715 Park Ave., New York 21)

7-9. Parapsychological Assoc., 4th annual congr., New York, N.Y. (C. B. Nash, St. Joseph's College, Philadelphia, Pa.)

7-10. Science News Writing Seminar, Colorado State Univ., Fort Collins. (M. G. Payne, Colorado State Univ., Research Foundation, Fort Collins)

7-11. European Orthodontic Soc., 37th congr., Bologna, Italy. (N. Gray, 16 College Rd., Eastbourne, Sussex, England)

7-12. Neurogenetics, symp., Rome, Italy. (L. Gedda, Istituto Gregorio

Mendel, Viale Regina Margherita 261, Rome)

7-13. Electroencephalography and Clinical Neurophysiology, 5th intern. congr., Rome, Italy. (R. Vizioli, Viale Università 30, Rome)

10-14. Tuberculosis Conf., 16th intern., Toronto, Canada. (C. W. L. Jeanes, 265 Elgin St., Ottawa, Ont., Canada)

10-15. Neurology, 7th intern. congr., Rome, Italy. (G. Alema, Viale Università 30, Rome)

10-17. International Union of Forest Research Organizations, 13th congr., Vienna, Austria. (Forest Research Inst., IUFRO Bureau, Vienna 89)

11-13. European Organization for Quality Control, 5th congr., Turin, Italy. (Weena 700, Rotterdam, Netherlands)

11-14. International Flax and Hemp Federation, 12th congr., Lisbon, Portugal. (IFHF, 37 rue de Courcelles, Paris 8)

11-15. Cosmic Rays, 7th intern. conf., Kyoto, Japan. (Y. Sekido, Science Council of Japan, Ueno Park, Tokyo)

11-15. Cybernetics, 3rd intern. congr., Namur, Belgium. (Intern. Assoc. for Cybernetics, 13 rue Basse-Marcelle, Namur)

11-15. Instrument Soc. of America, instrument-automation conf. and exhibit, 16th, Los Angeles, Calif. (W. H. Kushnick, 313 Sixth Ave., Pittsburgh 22, Pa.)

11-15. Marine Sciences Instrumentation, symp., Woods Hole, Mass. (D. D. Ketchum, Woods Hole Oceanographic Institution, Woods Hole, Mass.)

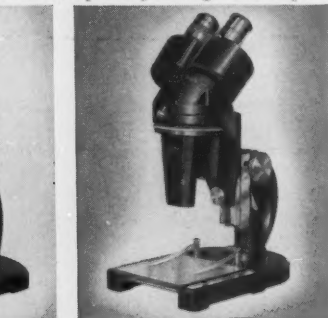
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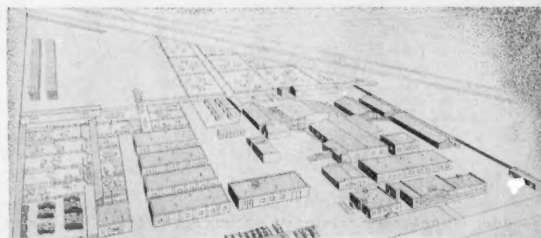
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